Agenda Item I

Sansum Santa Barbara Medical Foundation Clinic Request

California State Board of Pharmacy
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STATE AND CONSUMERS AFFAIRS AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
ARNOLD SCHWARZENEGGER, GOVERNOR

March 26, 2007

To: Members, Legislation and Regulation Committee

Subject: Request from Sansum Santa Barbara Medical Foundation Clinic Permit – Proposal

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At the January Board Meeting, John Cronin requested an opportunity to discuss an issue with one of the board's strategic committees.

A copy of his request is attached. I referred the matter to the Legislation and Regulation Committee, because the issue dealt with a law interpretation, and the Licensing Committee's agenda was full.

However, part of Dr. Cronin's request seems authorized by Business and Professions Code section 4126.5(a)(6) (copy attached).

Enforcement

DENNIS W. FREDRICKSON
TOMAS V. MAZEIKA *
TIMOTHY J. GRANT
PETER S. GREGOROVIC *
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ANDREW A. SERVAIS
STEPHEN B. HEATH
JONATHAN E. MEISLIN

January 30, 2007

Virginia Herold, Acting Executive Officer
California State Board of Pharmacy
1625 N. Market Blvd, Ste N219
Sacramento CA 95834

Re: Sansum Santa Barbara Medical Foundation Clinic Permits -- Proposal

Dear Ms. Herold:

In November I forwarded the enclosed proposal to Supervising Inspector Robert Ratcliff. The proposal is made to address the ongoing difficulties experienced by the Sansum Santa Barbara Medical Foundation Clinic because of the Board's current interpretation of the permit requirements for the Clinic.

Having received a negative response to our proposal from Inspector Ratcliff, we now feel the appropriate step to bring our proposal directly to the Board. We therefore request that our proposal be added to the agenda for the next meeting of either the Licensing or Enforcement Committee. Our hope is to reach some accommodation within the current law that will lessen the licensing burden which is negatively affecting the efficient operation and function of the Clinic.

The appropriate individuals from the Clinic are prepared to appear at the proper time to present the Clinic's proposal. Please advise us of the Committee to which our request has been assigned, as well as the date, time and location of their next meeting.

Sincerely,

John A. Cronin, Pharm.D., J.D.
For Sansum Santa Barbara Medical Foundation Clinic

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November 1, 2006

Robert Ratcliff, Supervising Inspector
California State Board of Pharmacy
1625 N. Market Blvd, Ste N219
Sacramento CA 95834

Re: Sansum Santa Barbara Medical Foundation Clinic Permits – Proposal

Dear Supervising Inspector Ratcliff:

Some time ago I contacted you about the desire of our client, the Sansum Santa Barbara Medical Foundation Clinic (SSBMFC), to restructure the various permits that they hold with the Board of Pharmacy. You suggested at the time that we prepare a proposal for review by the Board. Enclosed is that proposal.

If, after review, the Board has concerns about the approach we propose, we would like to meet and explore ways to resolve those problems. The intent of SSBMFC is to reach a better understanding of the concerns the Board may have and reach an agreement that can meet the needs of the Board.

The SSBMFC has asked me to represent them initiating discussion of this proposal. Please contact me if you need more specific information or if there are any questions. We look forward to your response to this proposal.

Sincerely,

John A. Cronin, Pharm.D., J.D.

Sansum Santa Barbara Medical Foundation Clinic
Proposal to State Board of Pharmacy
October 26, 2006

Background:
The Sansum Santa Barbara Medical Foundation Clinic (SSBMFC) is a non-profit, multi-specialty clinic owned and operated by a 501(c)(3) non-profit corporation. SSBMFC currently operates multiple clinic locations and contracts with 160 physicians and other medical providers. SSBMFC is exempt from licensure by the California Department of Health Services under Health and Safety Code section 1206(l).

SSBMFC currently holds the following permits from the California Board of Pharmacy:

Type	Location	Permit Number
Pharmacy (closed door)	215 Pesetas Lane Santa Barbara, CA 93110	PHY37310
Wholesaler	89 S. Patterson Santa Barbara, CA 93111	WLS4127
Clinic	215 Pesetas Lane Santa Barbara, CA 93110	CLN 1365
Clinic	317 N. Pueblo St. Santa Barbara, CA 93105	CLN1366
Clinic	51 Hitchcock Way Santa Barbara, CA 93105	CLN1367

- The wholesaler site is used to receive, warehouse and distribute bulk purchases of medical supplies and non-controlled legend drugs and devices for the "own use" of SSBMFC in its various clinics. The site serves as a central ordering, receiving and distribution hub for these products, which are primarily medical supplies, IV solutions, needles, syringes and various legend devices.

- The three clinic permit sites are not involved in dispensing. The clinic permits were obtained to accommodate the distribution of supplies and medicines for use in the medical practices that occur at these clinic sites.

- The pharmacy dispenses medications to SSBMFC patients and has served as a central receiving and distribution hub for some legend drugs. These drugs are distributed to the clinic sites upon the specific request of a medical provider and are for the "own use" of SSBMFC in its various clinics.

SSBMC has examined the current licensing requirements and believes modifications are in order as described in this letter. Their goal is to work with the Board to simplify the situation, arrive at a common understanding of how the clinics operate and to ensure compliance with the Pharmacy Law. SSBMFC is also seeking these modifications because of the new requirements for wholesalers, which will impose a significant and, in our view, unnecessary financial burden on the organization.

consistent with the federal Prescription Drug Marketing Act and the related federal regulations (21 CFR 203.3(cc); 64 Fed Register 67728-29, Dec. 3, 1999).

Conclusion

We believe the Pharmacy Law allows SSBMFC to conduct its current operations under our proposed set of permits; however, we do not want to conduct our operations in a manner that is inconsistent with the Board of Pharmacy's interpretation of the law. We therefore request a review of this proposal. We welcome the opportunity to meet with the Board to resolve any problems you may have with this approach with the ultimate goal of reaching an understanding of the law to which both of us can agree. If we are unable to reach such an understanding, we will consider pursuing a waiver from the Board to allow this approach.

We are eager to resolve this issue and revise our permits consistent with our proposal. Please contact me at your earliest convenience if further discussion of this proposal is needed.

WARNING: IF YOU ARE HAVING ANY UNEXPLAINED EYE DISCOMFORT, WATERING, VISION CHANGE, OR REDNESS, REMOVE YOUR LENSES IMMEDIATELY AND CONSULT YOUR EYE CARE PRACTITIONER BEFORE WEARING YOUR LENSES AGAIN.

(f) Any pharmacy and pharmacist dispensing replacement contact lenses shall be subject to all statutes, regulations, and ordinances governing the advertisement of contact lenses. In addition, any advertisement by a pharmacy or pharmacist that mentions replacement contact lenses shall include within the advertisement all fees, charges, and costs associated with the purchase of the lenses from that pharmacy and pharmacist.

(g) Any pharmacy dispensing replacement contact lenses shall register with the Medical Board of California at the time of initial application for a license or at the time of annual renewal of that license.

(h) All nonresident pharmacies shall maintain records of replacement contact lenses shipped, mailed, or delivered to persons in California for a period of at least three years. The records shall be available for inspection upon request by the board or the Division of Licensing of the Medical Board of California.

(i) The requirements of this section are applicable to nonresident pharmacies as defined in subdivision (a) of Section 4112. A nonresident pharmacy may dispense contact lenses only as provided in this section.

4125. Pharmacy Quality Assurance Program Required; Records Considered Peer Review Documents

(a) Every pharmacy shall establish a quality assurance program that shall, at a minimum, document medication errors attributable, in whole or in part, to the pharmacy or its personnel. The purpose of the quality assurance program shall be to assess errors that occur in the pharmacy in dispensing or furnishing prescription medications so that the pharmacy may take appropriate action to prevent a recurrence.

(b) Records generated for and maintained as a component of a pharmacy's ongoing quality assurance program shall be considered peer review documents and not subject to discovery in any arbitration, civil, or other proceeding, except as provided hereafter. That privilege shall not prevent review of a pharmacy's quality assurance program and records maintained as part of that system by the board as necessary to protect the public health and safety or if fraud is alleged by a government agency with jurisdiction over the pharmacy. Nothing in this section shall be construed to prohibit a patient from accessing his or her own prescription records. Nothing in this section shall affect the discoverability of any records not solely generated for and maintained as a component of a pharmacy's ongoing quality assurance program.

(c) This section shall become operative on January 1, 2002.

(Added Stats. 2000, Chapter 677)

4126. Covered Entity May Contract With Pharmacy To Provide Pharmacy Services; Segregation of Drug Stock; Return of Drugs not Dispensed; Wholesale License Not Permitted or Required

(a) Notwithstanding any other provision of law, a covered entity may contract with a pharmacy to provide pharmacy services to patients of the covered entity, as defined in Section 256b of Title 42 of the United States Code, including dispensing preferentially priced drugs obtained pursuant to Section 256b of Title 42 of the United States Code. Contracts between those covered entities and pharmacies shall comply with guidelines published by the Health

Resources and Services Administration and shall be available for inspection by board staff during normal business hours.

(b) Drugs purchased pursuant to Section 256b of Title 42 of the United States Code and received by a pharmacy shall be segregated from the pharmacy's other drug stock by either physical or electronic means. All records of acquisition and disposition of these drugs shall be readily retrievable in a form separate from the pharmacy's other records.

(c) Drugs obtained by a pharmacy to be dispensed to patients of a covered entity pursuant to Section 256b of Title 42 of the United States Code that cannot be distributed because of a change in circumstances for the covered entity or the pharmacy shall be returned to the distributor from which they were obtained. For the purposes of this section, a change in circumstances includes, but is not limited to, the termination or expiration of the contract between the pharmacy and the covered entity, the closure of a pharmacy, disciplinary action against the pharmacy, or closure of the covered entity.

(d) A licensee that participates in a contract to dispense preferentially priced drugs pursuant to this section shall not have both a pharmacy and a wholesaler license.

(e) Neither a covered entity nor a pharmacy shall be required to obtain a license as a wholesaler based on acts reasonably necessary to fully participate in the drug purchase program established by Section 256b of Title 42 of the United States Code.

(Added Stats. 2001, Chapter 631)

4126.5. Furnishing Dangerous Drugs by Pharmacy

(a) A pharmacy may furnish dangerous drugs only to the following:

(1) A wholesaler owned or under common control by the wholesaler from whom the dangerous drug was acquired.

(2) The pharmaceutical manufacturer from whom the dangerous drug was acquired.

(3) A licensed wholesaler acting as a reverse distributor.

(4) Another pharmacy or wholesaler to alleviate a temporary shortage of a dangerous drug that could result in the denial of health care. A pharmacy furnishing dangerous drugs pursuant to this paragraph may only furnish a quantity sufficient to alleviate the temporary shortage.

(5) A patient or to another pharmacy pursuant to a prescription or as otherwise authorized by law.

(6) A health care provider that is not a pharmacy but that is authorized to purchase dangerous drugs.

(7) To another pharmacy under common control.

(b) Notwithstanding any other provision of law, a violation of this section by either a pharmacy whose primary or sole business is filling prescriptions for patients of long-term care facilities or a person engaged in a prohibited transaction with a pharmacy whose primary or sole business is filling prescriptions for patients of long-term care facilities may subject the persons who committed the violation to a fine not to exceed the amount specified in Section 125.9 for each occurrence pursuant to a citation issued by the board.

(c) Amounts due from any person under this section on or after January 1, 2005, shall be offset as provided under Section 12419.5 of the Government Code. Amounts received by the board under this section shall be deposited into the Pharmacy Board Contingent Fund.

Agenda Item J

Pill Splitting

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STATE AND CONSUMERS AFFAIRS AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
ARNOLD SCHWARZENEGGER, GOVERNOR

Date: March 26, 2007

To: Legislation and Regulation Committee

From: Virginia Herold, Executive Officer, Board of Pharmacy

Subject: Issue of Pill Splitting

During the Subcommittee on Medicare Drug Benefit Plans on November 30, 2006, the committee was asked to consider the safety of pill splitting by patients. Charles Phillips, M.D., attended the subcommittee meeting and stated that he was concerned with the practice of pill splitting due to pills not splitting evenly, and the resultant crumbled residue of drug product in the bottom of pill containers.

Subcommittee Chairperson Goldenberg asked Dr. Phillips to provide information on this topic at a future board meeting. Dr. Phillips subsequently attended the board meeting held on January 31, 2007, and provided his testimony along with two handouts. Dr. Schell opened the floor for comments and discussion on the subject of pill splitting. Several speakers provided their comments.

The board referred the matter to (both) the Communication and Public Education Committee and the Legislation and Regulation Committee for further discussion and recommendation.

Attached are materials from the January 31, 2007 Board Meeting:

From BOP

- Excerpts from the (draft) minutes regarding the discussion on pill splitting

From Dr. Charles Phillips

- NABP 2nd Quarter 2000 newsletter containing an article entitled "Tablet-Splitting Policies Raise Concern"
- NABP Resolution No. 97-4-01 entitled "Opposition to Mandated Tablet Splitting"

From Dr. John Jones (United Health Care)

- Frequently Asked Questions from United Health Care entitled "Half Tablet Program – Effective August 15, 2006"

From Dr. Steven Gray (Kaiser Permanente)

- Various news articles and scientific research on the subject of pill splitting, including an article from Consumer Reports

EXCERPTS FROM THE DISCUSSION REGARDING PILL SPLITTING FROM THE (DRAFT) MINUTES OF THE JANUARY 31, 2007 BOARD MEETING

Chairperson Schell stated that during the Subcommittee on Medicare Drug Benefit Plans held on November 30, 2006, the committee was asked to consider the safety of pill splitting by patients. Board member Stan Goldenberg serves as Chairperson of the Subcommittee.

Charles Phillips, M.D., an emergency room physician, attended the Subcommittee on Medicare Drug Benefits Plans Meeting held on November 30th, and stated that he was concerned about the practice of pill splitting. Subcommittee Chairperson Goldenberg asked Dr. Phillips to provide information on this topic at a future board meeting.

Chairperson Schell called on Dr. Phillips to make his presentation on the subject of pill splitting.

Dr. Phillips introduced himself as an emergency room physician, currently practicing in Corcoran, California. He stated that he regularly fine tunes proper dosage medication for patients, teaches medication administration, and is experienced in titrating medication.

Dr. Phillips presented a bottle containing cholesterol medication, as a visual display. The bottle contained fragments and crumbled residue of drug product at the bottom of the container. Dr. Phillips stated that the crumbled residue was a result of pill splitting. He stated that he has not seen any books on the subject of pill splitting or pill fragmentation, yet the practice is commonplace.

Dr. Phillips stated that he wrote a prescription for himself for a 20-milligram dosage of medicine, and later presented that prescription to a Kaiser pharmacy to fill. The prescription that was filled and provided to him, however, contained a 40-milligram dosage. The medication was provided to him from the Kaiser pharmacy, along with a pill splitter. Dr. Phillips stated that he did not write the prescription that way. He expected 20-milligram dosage medication. He stated that the explanation given at the Kaiser pharmacy window was that it is their policy to provide the higher dosage pill to the patient, along with a pill-splitter.

Dr. Phillips stated that the policy to pill-split is carried out throughout Kaiser pharmacies, V.A.s, and some Medi-Cal units. He stated the policy is carried out for fear of retaliation, peer reviews, and pressure to save costs and increase profits, and that physicians are afraid to speak out. He questioned whether it is ethical to ask patients to pill-halve when there is a standard pill in the lower dose, particularly for patients who are physically incapable of performing an accurate pill split. He provided an example of a specific patient who has cerebral palsy. Mr. F. can move only his head, not his arms or legs, yet he has been asked to pill-split, which he is incapable of doing. When Mr. F.'s attendant is unavailable to perform a pill-split, he cannot take the proper dosage when needed, and that results in muscle pain and other problems.

Dr. Phillips stated that even when a prescription for a lower dosage is presented to a pharmacy, the pharmacy technician or pharmacist hits a button resulting in a higher dose medication, along with instructions to the patient that the pills must be split. He said there is no physician orientation book for Kaiser physicians on this policy.

Dr. Phillips asked Kaiser for any research they have to support their policy of asking patients to split pills. He stated that no research was provided from Kaiser as a result of his request, but they stated that the VA started the practice, and Kaiser adopted it. He further stated that Kaiser enjoys a budget savings as a result of the practice, and the VA experiences around $40,000,000 in cost savings with the practice of pill splitting. Dr. Phillips referred to a VA study of 442 reports of pill splitting, which resulted in 38 adverse medical events that were not therapeutic to patients. According to the survey, not all pills were split evenly. Inconsistent dosages resulted in medications causing higher reactions one day and lower reactions on other days, including bouncing cholesterol and blood pressure. He also referred to a study of 752 reports of pill splitting that showed 41 percent of the split pills deviated by more than the accepted weight standard.

Dr. Phillips recommended that the board take a stand on pill splitting and pill fragmentation. He stated that if the board is silent on this issue, it enables the problem. He considers the policy of asking seniors to pill-split is a form of patient abuse. Dr. Phillips referred to a case against Kaiser where the judge said he hadn't heard a lot of noise from regulatory bodies on the subject. He also referred to a 1997 NABP conference in Seattle that addressed the issue of informed consent regarding pill splitting and pill fragmentation. He believed that all 50 states participated in the conference.

Ms. Herold clarified that the California Board of Pharmacy was not a member of the NABP in 1997. The board has since joined, but was not a member at the time that Dr. Phillips stated.

Chairperson Schell opened the floor for questions or comments from the board and the public.

Mr. Goldenberg asked if any state's board had passed an informed consent rule regarding pill splitting.

Dr. Phillips stated that Kentucky's board came close, but only provided a general resolution on the subject of informed consent. He further stated that he has complained separately to California's Medical Board.

Dr. Hiura asked why physicians write these prescriptions when they are aware of the problems, especially when some manufacturers sell 10 milligrams for the same price as 20 milligrams or 40 milligrams.

Dr. Phillips responded that he does not write prescriptions that way, unless the patient specifically states that they cannot afford the medication and they must choose between the medication and food. In that case, Dr. Phillips will write the prescription and inform the patient as to the risks. He stated that Kaiser physicians cooperate with Oakland to become vested and retire, and Kaiser physicians shown the data would not pill-split without the policy.

Mr. Hough stated that he agreed with Dr. Phillips' concerns, and believed that the issue relates directly to the cost of health care.

Chairperson Schell asked if there were any other comments. Various comments were provided including reference to data from a study at Florida's College of Cardiology showing a safety efficacy window that was not affected by varying weights of split tablets. Dr. Ravnan said she believes the evidence supports a safe practice of pill splitting.

Steven Gray, Kaiser Permanente, provided a binder of printed documents for the board's review. The binder contained various news articles and scientific research on the subject of pill splitting. One of the documents was a copy of an on-line article about pill splitting from Consumer Reports. Dr. Gray stated that although Consumer Reports is not a scientific magazine, they base their recommendations on science. The article listed medications that can be safely split. Dr. Gray stated that physicians and scientists must make decisions on which medications are safe to split, and learn as we go, reversing decisions based on data as applicable. He said that pill splitting devices should be provided free of charge to patients to effectuate pill splitting which he said would be better than using a paring knife.

Dr. Gray further stated that pill splitting is performed nationally and internationally. The practice is encouraged by medical group committees. He stated that the program is voluntary. Dr. Gray said that informed consent would have four types of mandates:

1. on patient
2. on physician
3. on pharmacist
4. on pharmacy

President Powers asked what happens if a patient tells his or her doctor that he or she does not want to split a pill.

Dr. Gray responded that patients would then get the dose they need in a non-split form. But he couldn't guarantee that that practice would be followed by every physician. And he couldn't guarantee that every patient would split a pill, even when asked to do so.

Mr. Dazé commented that there appears to be an educational process in a 3-person chain: patient, doctor, and pharmacist. Mr. Dazé asked if each patient should be informed that he or she does not have to accept a split pill prescription.

Dr. Gray responded that a doctor should inform the patient that he or she does not have to accept a split pill prescription. The patient has the right to request the proper dosage.

Anthony Morielli introduced himself as someone who works for the VA, but was not representing the VA. He's a pharmacist and researcher in this area. He stated that he believes the facts about pill fragmentation are being distorted by Dr. Phillips. There are differences in clinical effects of any pill, and that 15 percent variation up or down in any individual dose is acceptable. Dr. Morielli took scored tablets approved by FDA for splitting and matched them to unscored lower doses – he said results show same variation – only 2 percent did not meet standard, and none exceed 17 percent of variation the range. Dr. Morielli advocated health care system cost savings, but did agree that safeguards should be in place. Pill splitting has its

benefits, and has limited clinical adverse events. At the VA, no one is mandated to split. In their computer system, medication will show as a pill-split dose, so doctor gives the patient counseling along with a pill splitter. Most patients go along with the program. Dr. Morielli asked that the board recommend that doctors apply good science, and give patients options and informed consent.

John Jones introduced himself, stating he was from United Health Care and had 30 years practice in tablet splitting. He didn't recall any negatives, except for discarding some split pills. He provided a handout from United Health Care that indicates that pill splitting is a voluntary program. He further stated that he is on the IOM panel to review the VA drug management system. He suggested a public education program for patients to know when it's appropriate and when it's not appropriate. For example, mental acuity of a patient could affect whether the patient could perform a pill split with accuracy. Cost savings are important to vets, as well as avoiding the Medicare Part D donut hole. Out of pocket costs are reduced by pill splitting. Dr. Jones asked the board to preserve the pill splitting tool.

John Cronin introduced himself as a private pharmacist and attorney in San Diego. He said that a point not raised is that this practice is driven by dollars. The issue belongs in public education. He further stated that Consumer Report articles end up in broadcasts, even on UCSF student fact sheets. Pill splitting can be safe, but the problem is that many consumers start wanting to split everything, including odd-shaped tablets like Lipitor, which are expensive. Dr. Cronin asked the board to keep the matter of informed consent in the Public Education Committee.

President Powers said he has tried splitting a soft small pill that falls apart when he tries to split it. He said there is evidence of problems with pill splitting, and that he will refer the matter to both committees (Public Education and Enforcement) for further recommendation.

2nd Quarter 2000

National Pharmacy

(Applicability of the contents of articles in the National Ph. y assumed and can only be ascertained by ex

IOM Report Addresses Medical Errors

A report released in late 1999 by the Institute of Medicine (IOM) of the National Academy of Science's Committee on Quality of Health Care in America concluded that rigorous changes throughout the health care system, including mandatory reporting requirements, are necessary to reduce medical errors and create a safer health care system.

Citing recent studies that place mortality estimates from medical errors between 44,000 and 98,000 annually, the Committee outlined a plan for government, industry, consumers, and health providers to reduce medical errors; called on Congress to form a national patient safety center to develop new systems that can address persistent problems; and set as a minimum goal a 50% reduction in errors over the next five years.

"Our recommendations are intended to encourage the health care system to take the actions necessary to improve safety," said William Richardson, chief executive officer of the W.K. Kellogg Foundation, Battle Creek, Mich, and chair of the Committee. "We must have a health care system that makes it easy to do things right, and hard to do them wrong."

The report, entitled "To Err Is Human: Building a Safer Health System," is available for a fee by calling 800/624-6242. The IOM is a private, nonprofit institution that provides health policy advice under a congressional charter granted to the National Academy of Sciences.

FDA Issues Final Dietary Supplement Labeling Rules

In the January 6, 2000 *Federal Register*, the US Food and Drug Administration (FDA) published final regulations that define the types of statements that can be made concerning the effects a dietary supplement has on the structure and function of the human body pursuant to the Dietary Supplement Health and Education Act of 1994 (DSHEA). The regulations are intended to clarify the types of claims that may be made for dietary supplements without prior review by the FDA, as well as the types of claims that require prior authorization through the establishment of criteria for determining when a statement about a dietary supplement is a disease claim.

Under DSHEA, dietary supplements may, without prior FDA review, carry "structure/function" claims (ie, claims that a product may affect the structure or function of the body), but may not, without prior FDA review, carry express or implied claims that they can treat, diagnose, cure, or prevent disease (disease claims). For example, the express disease claim "prevents osteoporosis" and the implied disease claim "prevents bone fragility in postmenopausal women" would be prohibited without prior FDA review. The rule clarifies that express and implied disease claims made through the name of the product (ie, Carpaltum, CircuCure); through a statement about the formulation of a product (ie, contains aspirin); or thorough the use of pictures, vignettes, or symbols (ie, electrocardiogram tracings) can be made. It also permits claims that do not relate to disease, such as health maintenance claims ("maintains a healthy circulatory system"); other non-disease claims ("for muscle enhancement"); and claims made for common, minor symptoms associated with life stages ("for common symptoms of PMS," "for hot flashes").

Under DSHEA and existing regulations, dietary supplement manufacturers are already required to maintain documentation substantiating structure/function claims and must include a disclaimer on their labels that their products are not drugs and receive no FDA pre-market approval. They must also notify the FDA of the claims they are making within 30 days of marketing.

The final rule became effective February 7, 2000. For further information contact Ann Marlin Witt, Office of Policy, Planning, and Legislation (HF-11), FDA, 5600 Fishers Lane, Rockville, MD 20857, 301/827-0084.

Tablet-Splitting Policies Raise Concern

Some state boards of pharmacy are concerned about the cost-saving initiatives of certain health care plans that encourage or mandate the practice of dispensing higher doses of certain medications so that patients must split the tablet to obtain the appropriate dose. Targeted are those high-cost drugs that are available in similarly priced higher- and lower-dose tablets, such as Zoloft®, which has 50 mg and 100 mg dosages selling for about the same price. Medical insurance plans favoring this method of cost cutting provide pill-cutters to enrollees and instruct physicians to prescribe the higher dosage tablets.

Inaccuracies in tablet splitting, the lack of testing on the effectiveness of split pills, and the potential for overdosing are the primary issues of concern. "As a cost-saving measure, tablet splitting may be considered in certain situations; however, health care insurers should not mandate such practices for financial gain without regard to patient safety," says NABP President Dyke F. Anderson. "The pharmacist is ultimately responsible for providing adequate patient counseling, and for assuring that tablet-splitting is safe and appropriate for the patient."

FDA Targets Illegal Internet Prescription Sales

The US Food and Drug Administration (FDA) is furthering its efforts to combat illegal Internet prescription drug and device sales. The agency recently announced that it has issued, via the Internet, warning letters to a dozen foreign-based Internet

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RESOLUTION NO. **97-4-01**

TITLE: **Opposition to Mandated Tablet Splitting**

Whereas, insurance companies and pharmacy benefit managers are advocating and mandating that practitioners prescribe and pharmacists dispense dosages of medications that may require the patient to physically split the medication; and

Whereas, the precise splitting of tablets may be difficult for patients, resulting in under- or overdosing and endangering patients' health; and

Whereas, the tablet splitting practices advocated and mandated by insurance companies and pharmacy benefit managers do not appear to be in the best interest of the patient but, rather, monetarily driven;

THEREFORE BE IT RESOLVED that NABP oppose this mandate by working with other national associations and government agencies to stop this potentially dangerous practice.

(Resolution passed at NABP's 97th Annual Meeting, Seattle, WA)

UnitedHealthcare®
A UnitedHealth Group Company

Half Tablet Program – Effective August 15, 2006
FREQUENTLY ASKED QUESTIONS

Q1: What medications are available for tablet splitting in the Half Tablet Program?

The list of medications available for tablet splitting includes:

Category	Medications	Dosage
ACE inhibitors	Aceon	2mg, 4mg
	Mavik	1mg, 2mg
	Univasc	7.5mg
Angiotensin Receptor Blockers (ARBs)	Atacand	4mg, 8mg, 16mg
	Avapro	75mg, 150mg
	Benicar	20mg
	Cozaar	25mg, 50mg
	Diovan	40mg, 80mg, 150mg
Antidepressants	Lexapro	25mg, 50mg
	Pexeva	10mg, 20mg
	Zoloft*	5mg, 10mg
Lipid-lowering medications	Crestor	5mg, 10mg, 20mg
	Lipitor	10mg, 20mg, 40mg
	Pravachol*	5mg, 10mg, 20mg, 40mg
	Zocor*	
Antivirals	Valtrex	500mg

* Half Tablet Program applies to the generic equivalents to these brands.

The list of medications available for tablet splitting does not include all medications within a therapeutic class; only those medications determined to be appropriate for splitting are included.

Some of the tablets included in this program are not scored or designed specifically to be split. However, with the use of a tablet splitter, these medications may be appropriately divided. As is true with all medical decisions, you and your doctor will need to determine if the Half Tablet Program is right for you. Medications in the program will be reviewed periodically; additional medications may be included as appropriate.

Q2: What are the criteria for determining which medications are included in the program?

The UnitedHealthcare National Pharmacy and Therapeutic (P&T) Committee approved the following clinical criteria to determine prescription product inclusion in the Half Tablet Program.

- Medications with a wide margin of safety so that minimal differences in tablet sizes will not result in either underdosing or overdosing
- Tablets that can be split relatively evenly without crumbling
- Medications that will remain stable after splitting

In addition, the medication must be available in "double" dosage strengths that are comparably priced.

The National P&T Committee approved the following criteria for exclusion of medications from the program.

- Enteric-coated tablets
- Capsules, liquids, topical medications
- Unscored extended-release tablets
- Combination tablets in which the amount of one active ingredient changes from one tablet to the next, but the amount of the other ingredient does not

Q3: How do I get my free tablet splitter?

You can call 1-877-471-1860 or visit www.halftablet.com to order your free tablet splitter and to view Frequently Asked Questions regarding the Half Tablet Program. Notification letters will contain a Participant Code which is required when ordering the tablet splitter.

Q4: How long does it take for my splitter to arrive?

Your splitter should arrive within 10 business days. Please do not call to check on the status of your tablet splitter until at least 10 business days. If you do not receive your splitter after 10 business days you may call 1-877-471-1860 for more information.

Q5: Can I still get a free tablet splitter if I don't have a Participant Code?

If you haven't received a letter, lost your letter, or do not have a Participant Code you can still receive one free tablet splitter by calling 1-877-471-1860. You will be asked to provide your UnitedHealthcare member number and your eligibility in the program will be verified. Not having a Participant Code may cause a delay in receiving your free tablet splitter.

Q6: What if lose my tablet splitter? What if it breaks or wears out?

Tablet splitters are available for purchase at most pharmacies. UnitedHealthcare will provide you with one free tablet splitter.

Q7: How does the program work?

If you fill a prescription for a medication included in the Half Tablet Program you will:

- Receive a notification letter in the mail informing you of the Half Tablet Program.
- Discuss the Half Tablet Program with your doctor. You and your doctor decide together if the program is appropriate for you. If yes, your doctor writes a new prescription for the higher-strength dosage with instructions to take one-half tablet.
- Fill your prescription at a participating retail pharmacy.
- Receive an appropriate quantity (15 tablets to meet 30-day supply, 16 tablets to meet 32-day supply, or 17 tablets to meet 34-day supply) with instructions for using half a tablet.
- Follow instructions included in member notification letter for obtaining free tablet splitter or purchase one at a retail pharmacy.

Q8: How does the Half Tablet Program work at mail order?

You will receive 45 tablets to meet a 90-day supply at mail order. Because prescriptions are dispensed as written through mail order, you must obtain an appropriately written prescription for participation. The mail order pharmacy will not make outbound patient or doctor calls to initiate program participation.

Q9: What if I don't want to participate in the program?

Participation in the program is entirely voluntary. If you do not wish to participate in the program, you may simply continue to fill your prescription as usual, taking the same strength dosage. No action is required if you choose not to participate. If you try the Half Tablet Program and decide that it is not right for you, you may have your doctor write a new prescription for the old dosage level and go back to your usual copay.

Q10: Have any studies been done on the safety and effectiveness of tablet splitting?

A number of clinical studies have been conducted on the safety and effectiveness of tablet splitting. These studies, published in peer reviewed medical literature, conclude that when appropriate medications are selected, tablet splitting delivers a safe and effective dose of medication. The following sections summarize two of the studies that have been conducted (please be advised the descriptions below are very clinical in nature).

Parra D et al. Effect of splitting simvastatin tablets for control of low-density lipoprotein cholesterol. American Journal of Cardiology 2005;95:1481-1483.
This is a retrospective evaluation of a voluntary simvastatin tablet splitting program in 6 VA medical centers. A total of 1,331 patients who were converted to split tablets and 2099 who were not converted were included in the analysis. Patients were converted from whole to split simvastatin tablets at the same total daily dose and issued a pill splitter and instructions about the conversion. Patients who had visual limitations or other disabilities were exempted from the conversion as were patients whose health care provider or pharmacist deemed them unable to perform the tablet splitting. Primary endpoints were the average final LDL-cholesterol value and the average change from baseline between the split group and the whole tablet group. Secondary endpoints included comparison of total yearly simvastatin costs between groups, incidence of transaminase increases greater than 2 to 3 times the upper limit of normal and assessment of compliance. Baseline and final LDL-cholesterol levels and average change from baseline were not significantly different between

groups (P>0.05), nor were the incidences of transaminase increases or measurements of patient compliance.

Gee M, Hasson NK, Hahn T, and Ryono R. Effects of a tablet-splitting program in patients taking HMG-CoA reductase inhibitors: analysis of clinical effects, patient satisfaction, compliance, and cost avoidance. Journal of Managed Care Pharmacy. 2002(8)6:453-58.
The primary objective of this study was to determine the effect of splitting atrovastatin, lovastatin, and simvastatin tablets on laboratory outcomes (lipid panel and liver enzyme tests). Other objectives were to assess patient compliance and satisfaction with splitting tablets and to measure the reduction in drug acquisition cost. Before entering the program, patients were evaluated by a prescribing physician or pharmacist for cognitive or physical barriers to assess whether or not hey were able to effectively split tablets. If patients agreed to participate, prescriptions were automatically converted by a pharmacist. A tablet splitter and instructions for use were provided free of charge to patients. A total of 2,019 patients were included in the trial conducted by a Veterans Affairs Health Care System facility. A total of 512 patients were eligible for the laboratory analysis. There was no difference between preintervention and postintervention laboratory values for total cholesterol and triglycerides. There was a statistically significant, but not clinically significant decrease in LDL (102 vs. 97, p<0.001) and increase in HDL (46 vs. 48, p<0.001), AST (26 vs. 28, p<0.001) and ALT (24 vs. 26, p<0.006) after the initiation of tablet splitting. A total of 454 patients responses to a mailed questionnaire (50%). Results showed that 84% believed that the tablet splitter was not difficult to use, 85% stated that split tablets were not harder to take compared to whole tablets, and 74% agreed that the tablet splitter was not too time-consuming or bothersome; 46% believed that it was easier to take medications when they did not have to split the tablets. Only 7% of the patients stated that tablet splitting had an effect on their willingness to take medications, and 7% stated that they missed more doses in a month while tablet splitting.

Other studies on tablet splitting include:

1. MA Veronin and B Youan. Magic bullet gone astray: medications and the internet. Science 2004: 305:481.
2. JM Rosenbergy et al. Weight variability of pharmacist-dispensed split tablets. J Am Pharm Assoc 2002; 42:200.
3. J Teng et al. Lack of medication dose uniformity in commonly split tablets. J Am Pharm Assoc 2002; 42:195.
4. JE Polli et al. Weight uniformity of split tablets required by a Veterans Affairs policy. J Manag Care Pharm 2003; 9:401
5. TJ Cook et al. Variability in tablet fragment weights when splitting unscored cyclobenzaprine 10 mg tablets. J Am Pharm Assoc 2004; 44:583
6. BT Peek et al. Accuracy of tablet splitting by elderly patients. JAMA 2002; 288:451
7. MC Duncan et al. Effect of tablet splitting on serum cholesterol concentrations. AM Pharmacother 2002; 36:205.
8. M Gee et al. Effects of a tablet-splitting program in patients taking HMG-CoA reductase inhibitors: analysis of clinical effects, patient satisfaction, compliance, and cost avoidance. J Managed Care Pharm 2002; 6:453.
9. JP Rindone. Evaluation of tablet-splitting in patients taking lisinopril for hypertension. JCOM 2000; 7:22.
10. RS Staffor and DC Radley. The potential of pill splitting to achieve cost savings. Am J Manag Care 2002; 8:706.
11. P Gupta and K Gupta. Broken Tablets: does the sum of the parts equal the whole? Am J Hosp Pharm 1988; 45:1498.
12. JT McDevitt et al. Accuracy of tablet splitting. Pharmacotherapy 1998; 18:193.

UnitedHealthcare
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View a list of Frequently Asked Questions for UnitedHealthcare's Half Tablet Program.

You need Adobe Reader installed on your computer in order to view the Frequently Asked Questions. If you do not have it, you may click below for a free download.

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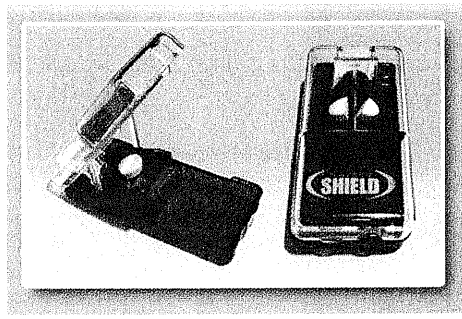

To order your FREE tablet splitter as part of the UnitedHealthcare Half Tablet Program simply type in the Participant Code and your name as it appears on your Half Tablet Program notification letter and click submit. Only one tablet splitter per particpant.

Participant Code | First Name | Last Name

Submit

☐ I have read and acknowlege the statement below

United Healthcare Services, Inc. ("United") is providing this free tablet splitter to you at your request. By ordering this tablet splitter, you acknowledge and agree that you will only use it to split tablets that your doctor has approved for splitting.

To help maintain the effectiveness of your medication, do not split all of your tablets at one time. Split one tablet and take one half. Take the second half for your next scheduled dose. Repeat the process until you have taken all of your medication.

This tablet splitter is not manufactured by United or any of its affiliates. United makes no warranty as to the reliability of the tablet splitter, nor does United guarantee or warrant the performance of the tablet splitter, including the tablet splitter's conformity to any law, rule, regulation or policy. You assume full responsibility for using the tablet splitter for its intended use in accordance with the manufacturer's instructions. United is not responsible for any direct, indirect incidental, consequential or punitive damages arising out of your use of this tablet splitter.

CON Pill-Splitting

Ken B James
08/30/2002 08:14 AM

To: DWNY DIS LIST-KPSC-SCAL
cc:
Subject: SF Chronicle - Today's News - Study finds pill splitting safe

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Ambrose Carrejo
08/30/2002 08:09 AM

To: PHM DECs-KPNC
cc: DUM Team-KPNC
Subject: SF Chronicle - Today's News - Study finds pill splitting safe

Some good news
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cc: Stacey Olvera/CA/KAIPERM@KAIPERM, David Campen/CA/KAIPERM@KAIPERM, Ambrose Carrejo/CA/KAIPERM@KAIPERM, Fred Hom/CA/KAIPERM@KAIPERM, GG PandT Chiefs-KPNC
Subject: SF Chronicle - Today's News - Study finds pill splitting safe

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08/30/2002 07:53 AM
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Subject: Today's News - Study finds pill splitting safe

Today's News

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San Francisco Chronicle
NORTHERN CALIFORNIA'S LARGEST NEWSPAPER

Study finds splitting pills usually is safe

By Ron Winslow
Reprinted from the Wall Street Journal
San Francisco Chronicle
Friday, September 1, 2002

The practice of splitting pills to save money on prescription drugs could lead to significant cost savings without risking the effectiveness of the medicines or the safety of patients, researchers say in a new study.

But doctors, health plans and patients should limit the practice to pills that, for both their price and the way they are made, lend themselves to it.

"You need to make sure it's done accurately, with full discussion between patients and physicians," says Randall Stafford, assistant professor of medicine at Stanford University's Center for Research in Disease Prevention and lead author of the study, which appears in the current issue of the American Journal of Managed Care. That being said, pill-splitting "can provide cost savings without really changing the clinical care that patients are getting," Dr. Stafford says.

Economic benefits of the strategy can be considerable. Kevin Graham, a cardiologist at Minneapolis Heart Institute in Minnesota, says prescribing 40 milligram tablets of the cholesterol-lowering drug Zocor for patients who then take just 20 milligrams a day by breaking the pill in two can save $730 a year.

"These people are often taking not one but three or four or five drugs that each cost from $1 to $4 a day," Dr. Graham says. "If you can get them a deal you become their friend."

But if patients, health insurers and employers see pill-splitting as an antidote to the soaring cost of drugs, the pharmaceutical industry sees otherwise.

Big drug companies have consistently warned that the practice could pose a risk to patients by leading to improper or inconsistent dosing and other problems. Kaiser Permanente, a big health-maintenance organization based in Oakland, Calif., that encourages pill-splitting with selective medicines, is defending itself in a lawsuit filed on behalf of some of its members seeking to end the practice.

Dr. Stafford's study is one of the few to examine the safety question and to set out criteria for determining which pills are best suited to cutting.

Dr. Stafford considered a list of 256 medicines commonly prescribed nationally and particularly at a small health plan in Boston during nine months in the year 2000. He and his co-author, David Radley of the Institute for Health Policy at Massachusetts General Hospital in Boston, winnowed them down to a list 48 medicines that could be split. But only 11 were prescribed often enough in the health plan to be found both clinically appropriate and cost-effective for the splitting strategy.

"It's important to note that it's a minority of medications that fall into this category," Dr. Stafford says. Yet he believes the potential for cost savings is substantial because drugs for high blood pressure and high cholesterol as well as antidepressants -- all widely used medications -- were on the final list.

Those on the list include the cholesterol reducer Lipitor and the impotency remedy Viagra, both marketed by Pfizer Inc.; the antidepressants Paxil from GlaxoSmithKline PLC and Celexa from Forest Laboratories Inc.; and the ACE inhibitor lisinopril, marketed as Prinivil by Merck & Co., and as Zestril by AstraZeneca PLC. (Lisinopril just went off patent and thus wouldn't likely now be a cost-effective candidate for pill-splitting.)

The economic advantage results from the fact that many drug companies charge essentially the same price per tablet regardless of the dose. That's to ensure that doctors don't have to factor in price when prescribing a dose to their patients, says Marjorie Powell, assistant general counsel at Pharmaceutical Research and Manufacturers of America, the industry's Washington-based trade group.

In developing their list of medicines suitable for splitting, Dr. Stafford and his colleague sought those with characteristics making them particularly easy to break in half, such as pills that are scored. They eliminated 125 drugs that either came only in one dose, were available only in a capsule, were prepackaged or weren't available in pills at all. These criteria eliminated such drugs as the heartburn remedy Prilosec, the osteoporosis pill Evista and common asthma medications that are dispensed in inhalers.

An additional 61 pills were eliminated because the potential cost savings to be derived from splitting weren't worth the effort; 31 others were ruled out because they were time-release formulations or out of concern of adverse consequences if dosage varied to any significant extent.

"It's important for both consumers and managed-care organizations to note that pill-splitting is a strategy that needs to be used selectively," Dr. Stafford says.

The drug-industry group challenges the strategy. Ms. Powell says she isn't convinced consumers are able to accurately split pills and that symptoms of heart disease and depression often require diligent efforts to get patients on the right dose of the right drug -- something splitting the medicines could undermine.

"It clearly isn't consistent with Food and Drug Administration labeling because you don't know exactly what dose the patient is getting," she says. If a doctor urged any of her family members to consider splitting their pills, she says, "I would make sure (they) changed doctors."

At Kaiser, Tony Barrueta, senior counsel, says officials remain confident in the clinical and economic wisdom of pill splitting despite the lawsuit. "You have to do it right," he says. "But it just makes a lot of sense."

Posted on Sun, Sep. 29, 2002

Splitting pills considered as way to cut costs

By TONY PUGH
Knight Ridder Newspapers

WASHINGTON - In the scramble to cut rising prices for prescription drugs, consumers and insurers are taking a new look at an old but controversial practice - splitting pills in half.

Purchasing large amounts of medications in high doses and cutting them in half saves money because bigger-dose pills of many drugs often sell for the same price or only slightly more than smaller doses.

Consumers can purchase 30 10-milligram doses of the antidepressant Paxil for $72.02 at Drugstore.com, for example. The site sells the same number of 20-milligram doses for $76.80. Cost-conscious customers can buy the larger-dose pills, split them in half and get twice as much medication for $4.78 more.

Pill splitting is not without risks. Because they may suffer from physical, mental or emotional problems, not all patients can correctly split their pills.

And not all pills should be split. Some must remain intact to be absorbed properly. Others can't be split accurately because of their shape. Even tablets with scores - those small grooves down the center - don't always split evenly, which could result in over- and under-dosing.

But with prescription-drug spending projected to jump 13.5 percent this year to $161 billion, health-care plans are warming to pill splitting as a low-tech method to curb rising drug costs.

The Veterans Affairs Department allows pill splitting for its patients. Last week, the Illinois Medicaid program began requiring patients who take the antidepressant Zoloft to purchase higher-potency pills and split them in half. Since 100-milligram Zoloft tablets cost about the same as the 50-milligram pills - $2.79 vs. $2.73 - the state will reimburse pharmacies only for the higher dose.

The move will trim about $3 million off Illinois' projected $1.4 billion Medicaid drug budget, said program spokeswoman Ellen Feldhausen. Private insurers such as Kaiser Permanente, United Healthcare, Health Net and Wellpoint Health Network also have voluntary policies allowing doctors to permit pill splitting if patients approve.

"I think it's inevitable that health plans will take a closer look at this. When they do so will vary and be determined by their own needs," said Dr. Randall Stafford, a professor of medicine at Stanford University who recently studied the cost-saving potential of pill splitting.

The savings must be balanced against the risks of improper dosage. A recent study of 11 commonly split tablets found that eight, after splitting, did not meet industry guidelines for content uniformity - between 85 percent and 115 percent of the intended dose. Even scored tablets did not assure accurate dosages.

For these reasons, groups such as the American Medical Association, the American Pharmaceutical Association and the American Society of Consultant Pharmacists have opposed mandatory pill-splitting

policies by health plans.

But if the doctor, patient and pharmacist all agree that pill splitting is workable, the practice can be safe on a voluntary basis, said Susan Winckler, vice president for policy with the pharmaceutical association in Washington.

Stafford's research, which tracked prescription records on 11 drugs, found that a Massachusetts HMO with 19,000 members could have saved nearly $260,000 a year by having its clients regularly split pills. Savings ranged from 23 percent to 50 percent, depending on the medication, Stafford said.

Tom Clark, director of professional affairs for the American Society of Consultant Pharmacists, said Stafford's study overstated the cost savings and understated the risks. He said there had been no studies on the health of patients who split pills.

"Our position is that it's irresponsible to promote this practice without any studies to show it's safe," Clark said.

For years, many people have split their regular-dosage tablets with razors, knives and pill-splitting devices to stretch their prescriptions when they couldn't afford refills. Groups such as the AARP frown on the practice, because patients don't get the proper dosages.

Kaiser Permanente, an Oakland, Calif.-based HMO, has been the industry leader in splitting higher-dose pills since it adopted the practice on a patient-voluntary basis in the early `90s. In 1999, Kaiser was sued over the practice; several patients and a Kaiser physician claimed that patients were being forced to split pills. Kaiser denies the allegation. The lawsuit is expected to go to trial next year.

Dr. Charles Phillips, an emergency-care physician in Fresno, Calif., and a former Kaiser physician, is a plaintiff in the lawsuit. While working for Kaiser, Phillips said, he frequently saw patients with diabetes and hypertension whose health was harmed by inaccurately split medications. He still opposes the practice because of the potential for error.

"It's bad medicine," Phillips said. "It saves money at that moment in time, but if the patient gets worse (because of improperly split dosages) then society is losing money, because they've got to pay for the patient's care down the line."

Kaiser officials, who have continued the practice of pill splitting, said the Stanford study validated it.

"It confirms our view, which is that a well-designed tablet-splitting initiative has the potential to improve cost-effectiveness of care without impairing quality," said Tony Barrueta, senior counsel for Kaiser.

ON THE WEB

For more information about pill splitting, go to the American Society of Consultant Pharmacists Web site, at www.ascp.com/public/pr/policy/tabletsplitting

THE WALL STREET JOURNAL. ONLINE

August 30, 2002

HEALTH

Study Finds Splitting Pills Usually Safe, Saves Money

By RON WINSLOW
Staff Reporter of THE WALL STREET JOURNAL

The practice of splitting pills to save money on prescription drugs could lead to significant cost savings without risking the effectiveness of the medicines or the safety of patients, researchers say in a new study.

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Drug prices are spiraling out of control. Read the series of Page One stories[1] on the embattled pharmaceutical industry.

HEALTH INDUSTRY EDITION

For more health coverage, visit the Online Journal's Health Industry Edition at wsj.com/health[2], and take a tour[3] of the edition.

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Write to Ron Winslow at ron.winslow@wsj.com[4]

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(4) mailto:ron.winslow@wsj.com

Updated August 30, 2002

Evaluation of the Reproducibility of Tablet Splitting to Provide Accurate Doses for the Pediatric Population

Lori W. Horn, Robert J, Kuhn, Jamshed F. Kanga

Abstract

Portions of tablets are commonly administered to pediatric patients with virtually no data to demonstrate that the correct dose is consistently delivered to the patient. This study was conducted to assess the reproducibility of tablet splitting with two different commercially available tablet splitting devices. Twenty tablets were randomly selected and split into halves and, if clinically appropriate, into quarters. Each part was weighed and assessed for statistically significant differences. Tremendous variability was found to exist between doses. Some tablet parts could not be reproducibly cut into parts with either cutter. Therefore, it was concluded that solid dosage forms should not be cut, especially into quarters. Patients cannot be assured of receiving the prescribed dosage on a consistent basis.

Introduction

Children are especially exposed to the dangers of medication errors. The risk of drug administration errors is high in the pediatric population due to differing age, size, and development and function of organs, such as the liver and the kidney. Pediatric dosages must be calculated on a weight basis, such as milligram per kilogram, or by body surface area. Certain drugs may not be readily available in suitable formulations, strengths, and concentrations for pediatric patients. Consequently, the risk of medication errors in these patients is increased since often the alteration of available dosage forms is required.[1-3]

The difficulty in assuring the delivery of an accurate dose of liquid medication has been appreciated.[4] There are occasions when a fraction of a solid dosage form may be required. Issues related to tablet splitting include: homogenous distribution of active ingredient, the point at which an unscored tablet should be split, and the most appropriate device for splitting tablets. Although portions of tablets are commonly administered to pediatric patients, it is done with virtually no data to support these actions.[5-6]

Only two studies have attempted to address these questions. Stimpel, et al.[5] evaluated fourteen brands of antihypertensive agents to determine how evenly the tablets would break along the scoring line. Most tablets broke easily, but deviations in half-tablet weights of up to 10% were frequent. Another study conducted by Sedrati, et. al.[6], examined the accuracy of a tablet splitting device with various shapes and sizes of tablets. They found the device was most accurate with larger tablets (> 600 mg), oblong tablets, and those that had flat edges.

We conducted a study with captopril, clonidine, amlodipine, atenolol, carbamazepine, and sertraline tablets to assess the reproducibility of tablet splitting using two different commercially available pill cutters. Tablet halves were evalu-

Lori W. Horn, Pharm.D., Moose Professional Pharmacy, Concord, NC. At the time of this writing Dr. Horn was a Clinical Pharmacy Resident, University of Kentucky, Lexington, KY
Robert J. Kuhn, Pharm.D., Professor, College of Pharmacy University of Kentucky, Lexington, KY
Jamshed F. Kanga, M.D., Professor, College of Medicine, University of Kentucky, Lexington, KY

ated for all medications and quarters were evaluated with clonidine and captopril. The purpose of this study was to determine whether a statistically significant difference between tablet parts could be demonstrated.

Methods

Drugs to be evaluated were chosen by surveying physicians at our institution to determine what tablets they were commonly seeing split into parts. The chosen medications are listed in the Table. Three lots were obtained for each medication. Capoten® (captopril) and clonidine were provided by their pharmaceutical manufacturers. All other medications were obtained from the University of Kentucky outpatient pharmacy. After an initial practice session, two sets of twenty tablets were randomly selected from each lot, individually weighed on a Mettler AT201 analytical balance (sensitivity to 10 μg) (Mettler Instrument Corporation, Highstown, NJ), and split with two different commercially available pill cutters into halves and into quarters if appropriate based on usage. Each part was weighed on the analytical balance. For simplicity, these cutters will be referred to as the "beige" cutter (EZ Dose, Bumsville, MN) (Figure 1) and the "blue" cutter (Health Care Logistics, Inc., Circleville, OH) (Figure 2). A new pill cutter was used for every one-hundred cuts to minimize any variation due to dulling of the blade. If a tablet was scored, an attempt was made to place the tablet in the cutter so that the blade would cut along the scoring line. If the tablet was not scored, the tablet was placed on the designated area in the cutter, and cut as close to the center as possible. Obvious physical and visual differences between tablet parts were noted by an independent observer. Homogenous distribution of the active ingredient throughout the entire tablet was assumed.

Descriptive statistics were used to assess the mean and the standard deviation of total tablet weight, the weight of the half, and the weight of the quarter. Normality of data distribution was assessed via observation of the similarity or closeness between standard deviations and was determined to be normally distributed. A two-tailed t-test, therefore, was used to test for differences between tablet halves. To test for differences between tablet quarters, a one-way ANOVA was used. A p value of < 0.05 was considered significant.

To address the uniformity of dosage units,[7] the USP may consider an analytical assay of the active ingredient to be the most appropriate method to assess differences between tablet parts. A practical measure, however, examining weight variation between tablet parts was employed in this trial.[7] If the variation in tablet weight is statistically significant, it could be deduced that the fraction of active ingredient delivered would be different for each part. Also, according to USP, to meet the uniformity of dosage unit requirements,

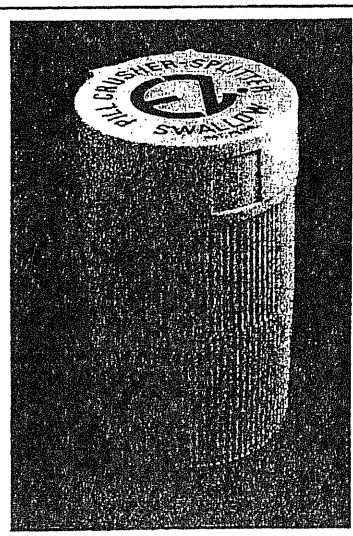

Figure 1. "Biege" cutter (EZ Dose, Bumsville, MN)

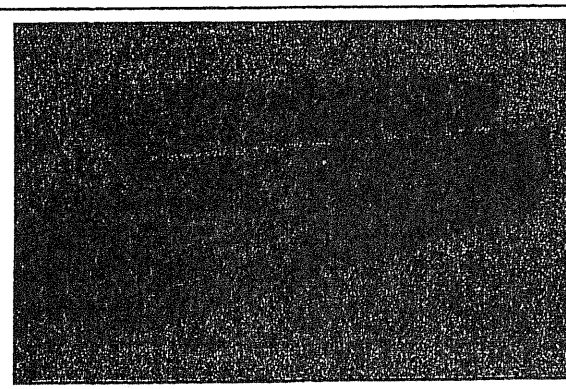

Figure 2. "blue" cutter (Health Care Logistics, Inc., Circleville, OH)

Table

Drug	Lot	Blue Cutter				Biege Cutter			
		% halves weighing within ± 15%	p-value	%quarters weighing within ± 15%	p-value	% halves weighing within ± 15%	p-value	% quarters weighing within ± 15%	p-value
[1]Catapres 0.1mg[S]	63003B	81.3	< 0.001	47.5	< 0.001	90.0	0.725	68.8	0.628
(136mg ± 1.91)	63002C	52.5	< 0.001	43.8	< 0.001	85.0	0.010	71.3	0.158
	064001B	100.0	< 0.001	60.0	< 0.001	90.0	0.001	57.5	0.076
[2]Clonidine 0.1mg[S]	2572-038	55.0	< 0.001	45.0	0.001	78.9	0.013	31.6	0.163
(70.06mg ± 2.16)	058H32	47.5	< 0.001	41.2	< 0.001	62.5	0.159	48.8	0.341
	130C41	70.0	< 0.001	37.5	< 0.001	30	0.006	25.0	0.013
[3]Capoten 12.5mg[S]	MAE015	67.5	< 0.001	37.5	< 0.001	95.0	0.053	28.8	0.084
(51.65mg ± 0.55)	MCE026	58.3	< 0.001	48.6	< 0.001	100.0	0.027	36.1	0.005
	L3J26A	95.0	< 0.001	55.0	0.007	100.0	< 0.001	26.3	0.003
[4]Amlodipine 5mg[NS]	D223D	85.0	0.002			90.5	0.417		
(199.5mg ± 2.39)	H121A	85.7	0.120			76.9	0.009		
	A863H	77.5	0.040			77.5	0.070		
[5]Tenormin 25mg[NS]	HA181	95.0	0.345			35.0	< 0.001		
(58.5mg ± 1.00)	HA051	62.5	< 0.001			27.5	0.009		
	HA201	87.5	0.012			25.0	0.012		
[6]Sertraline 50mg[S]	A593F	100.0	0.408			100.0	0.463		
(155.5mg ± 2.5)	F533A	100.0	0.076			100.0	0.101		
	3JP050A	100.0	0.495			90.0	0.001		
[7]Tegretol 100mg[S]	1T168197	92.5	0.1098			65.0	< 0.001		
(405.2mg ± 4.66)	1T160545	92.5	0.006			80.0	< 0.001		
	1T165813	87.5	0.215			60.0	0.099		

S = Scored into halves; NS = Not scored

1. Boehringer-Ingelheim Pharmceuticals, Inc., Ridgefield, CT
2. Rugby, Norcross, GA
3. Bristol-Meyers Squibb Co, Princeton, NJ
4. Pfizer LAbs, New York, NY
5. Zeneca Pharmaceuticals, Wilmington, DE
6. Pfizer, Roerig Division, New York, NY
7. Ciba Geneva, Summit, NJ

dosage units must contain within ± 15% of their label claim and the relative standard deviation must be < 6%.[7] Therefore, a significant difference was also represented by tablet parts which fell outside the ± 15% of the desired mean percentage of label claim.

Results

Statistically significant differences were demonstrated when cutting clonidine tablets into halves (p-values < 0.001). (Table) The brand name, Catapres®, reproducibly cut better than the generic clonidine. In fact, one lot of the brand name clonidine (Catapres®) demonstrated the ability to be reliably split into parts, as 100% of tablet parts fell within the desired specifications of ± 15% of the desired weight. The range was 52.5% to 100%. In contrast, 78.9% of the generic clonidine tablet halves fell within the desired specifications at best case and only 30% at worst case. As a general rule, fewer than 50% of quarters were within USP accepted standards. Similar results were obtained with captopril tablets.

In general, the beige cutter appeared to be more accurate when cutting halves. However, neither cutter demonstrated satisfactory results when cutting quarters. Statistical analysis to determine the superiority of one tablet splitter over the other was not conducted, because neither splitter reproducibly cut tablets into the desired parts.

Because of the tremendous variability observed in phase one between tablet quarters, tablets in the second phase of this study were only split into halves. (Table) As in the first phase of this study, all of the drugs, except sertraline, could not be reproducibly cut into halves. In fact, only 25% to 35% of Tenormin® (atenolol) tablet halves weighed within ± 15% of the desired mean percentage of the total tablet weight. Unlike the first phase, the beige cutter yielded less reproducible results than did the blue cutter. However, neither cutter yielded consistent results.

Obvious physical differences could be observed in greater than 50% of tablet halves. Some tablets, such as Tegretol® (carbamazepine) 100mg chewable tablets, even crumbled into multiple pieces when split into parts. The pieces were weighed together as accurately as possible, unless the tablet was pulverized.

Discussion

Enormous variability exists between doses when tablets are halved or quartered. This data likely represents the best case scenario with respect to the accuracy of tablet splitting. In the real world, tablets are split by parents into parts with knives, razor blades, fingers, and other such devices. Occasionally, parents may have a tablet splitting device available to them. However, even with these devices, the inability for tablets to be reproducibly split into a desired part has been demonstrated. Moreover, if the assumption that the active ingredient is homogeneously distributed throughout a tablet is not valid, the potential for even larger variation in dosage exists. Although no pharmaceutical company will guarantee homogenous distribution of active ingredient, even for scored dosage forms, it is assumed daily by physicians and pharmacists. Analytical studies would be required to evaluate this further.

Pediatric practitioners and pharmacy administrators need to evaluate their policies and beliefs regarding the manner in which small dosages are delivered to pediatric patients. Alternative dosage forms should be investigated. Extemporaneous compounding of solutions, suspensions, suppositories, or powder papers may be required. For example, due to the significant variability demonstrated with captopril, these tablets are no longer cut into parts at our institution. In light of a recent study of captopril in solution,[8] we are now dispensing only liquid dosages of captopril to our pediatric patients.

Clonidine was chosen in this study to examine the clinical dilemma of delivering small doses (e.g. 25µg by mouth) to our pediatric patients with attention deficit hyperactivity disorder. This therapy is being used more frequently for many pediatric patients.[9] Dosing variability (e.g. differences in tablet weight) could affect the ability to assess successful drug therapy for this condition. Differences in tablet size and manufac-

turers for a given product may exacerbate these differences and complicate patient assessment. The approximate twofold greater initial tablet weight and size of Catapres® may explain the increased variability observed with generic clonidine.

A follow-up prospective evaluation of whether a correlation exists between variations in dose and clinical outcomes would be informative. This information would allow the full implication of the dosage variations to be appreciated. Until this information is known, however, tablets should not be split into parts for pediatric patients. Tablets should not be cut, especially into quarters. Patients cannot be assured of receiving the prescribed dosage on a consistent basis. The ultimate effect of this variation on patient outcome, however, remains to be determined. If tablets are split the health care team needs to carefully evaluate the patient and take into consideration this dosage variability in the desired outcome of their patient.

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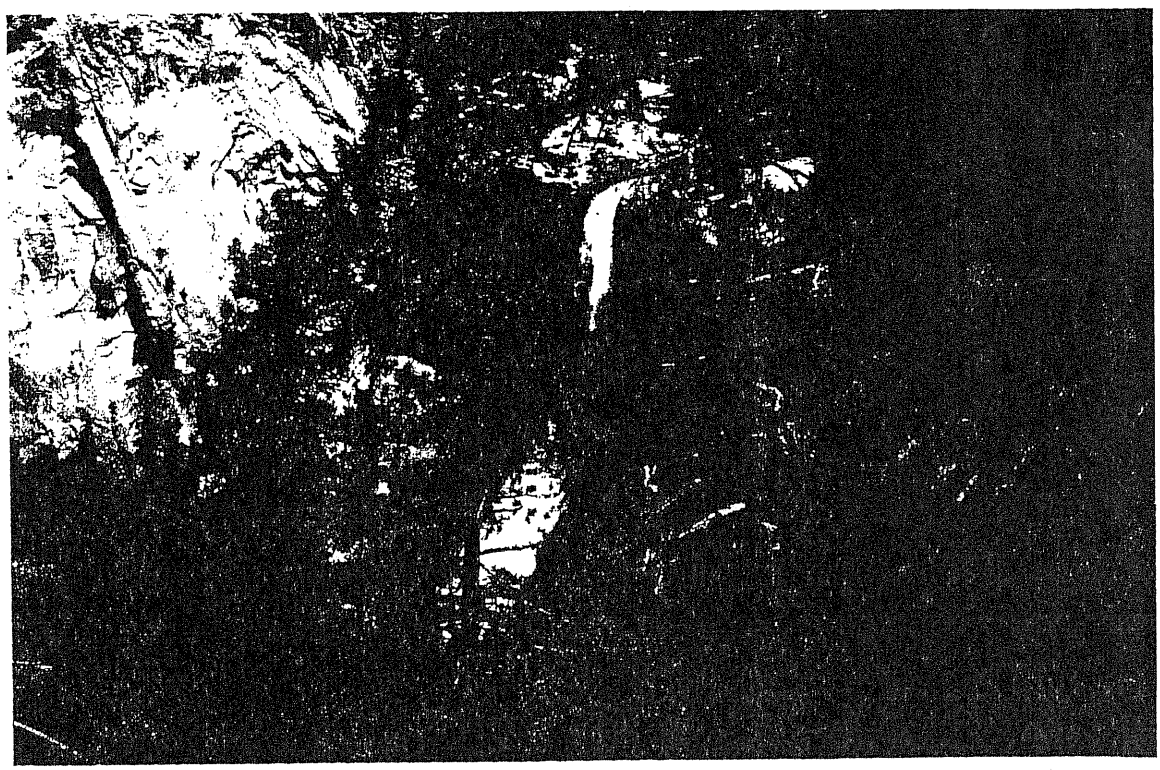

Nevada Falls, Yosemite National Park, CA

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"Pill Fragmenting Program" -

Presentation by Charles Phillips, MD of Fresno, California
On Invitation to Speak at the California Board of Pharmacy
San Diego Meeting on January 31, 2007

INTRODUCTION

I would like to thank the Pharmacy Board's Subcommittee on Medicare Drug Benefits Plan for inviting me,[1] a physician, to discuss pill fragmentation before the full Board today. It is appropriate that this presentation be in San Diego for it is here that pill splitting got its start [2] and, perhaps, where it should as massive programs be stopped.

I also have to thank Maggie Dee for helping me to understand this problem through the disabled patient point of view as well. One patient she helped me to meet by Email is Mr. Nick Feldman, who due to cerebral palsy can only move his head. Yet he has graduated from UC Berkeley. He has been forced by Kaiser to split pills – Zanaflex 4 mg into two pieces that are supposed to simulate the 2 mg tablet. He saw the fragments created by his attendant's best efforts and stopped the splitting. He takes the whole dose in the morning to avoid the humiliation of medication fragmenting. This means he is over sedated in the morning and has muscle cramps in the afternoon. He has asked – through an Email to me – that you listen to me today and take action soon; he knows what is going on and wants it to be stopped.[3]

I believe large scale "pill splitting" to be a form of general patient abuse; it is particularly obnoxious to force onto the disabled. It is a form of **senior abuse.**[4] It is also - in its

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[1] My friends would find me well qualified to talk about HMOs and medications – as I have written a whole chapter of one of my textbooks on "Medication Administration" [Exhibit #1]. I have taught the same topic to nurses and paramedics as well. My enemies would try to destroy me as a messenger by pointing to a tattoo on my medical license around not catching a physician assistant's poor evaluation on a child in 1999. Luckily all peer reviews of that incident have been in my favor, and I never lost being Board Certified in Emergency Medicine – now for my 25th year.

[2] Pill splitting began with Dr. Anthony Morreale at the VA in San Diego. Later he became the "Pharmacist Benefit Manager" for VISN 22 – the whole West Coast as pill splitting spread to the VA in Long Beach. Then it spread to Kaiser through Dr. Fawell who moved from the VA in Long Beach to Kaiser Vallejo. The VA has conceded that the pills split unevenly. Thus many have the vets split one pill every two days so that big and little fragments might be matched up (e.g. Tampa, Florida VA).

[3] One of the tricks used by Kaiser is to use two formularies – one for outpatient care that shows only one size for many medications – like Zanaflex 4 mg, Maxzide full strength, etc. The other one is seen by very few eyes but is built into the in-hospital dispensing systems with variable doses so that nurses are almost never asked to split pills. Zanaflex 2 mg is available in the Kaiser Hospitals. The traveling nurses – with no dental benefits – would be the first to turn Kaiser in for pill chopping if it occurred in the hospital. So if it is not safe for a nurse, how does that make it safe for a patient?

[4] Naturally, I do not object to the few cases where pill splitting is necessary – titration on the way to the correct dose, getting a patient through a weekend when a pharmacy is out of a medication, or helping a

HMO form - the illegal corporate practice of medicine by the top hierarchy[5] of the for-profit physician partnership[6] called the Permanente Federation.

Pill fragmentation or chopping results in **uneven fragments producing uneven treatment.**[7] In the case of the Kaiser HMO called "Kaiser Permanente"[8] this puts the risk of accelerating cardiovascular and depression illnesses onto the patients – opposite to the $45 million a year ad campaign with its "Thrive" message [Exhibit #4]. And nowhere in Kaiser's ads or website are seniors – the most vulnerable - warned that they might be funneled[9] into pill splitting schemes or just what uneven pill fragments mean.

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patient (like a child) achieve a correct medication dosage where there is no manufactured alternative. Pill scores were never meant to be invitations for massive pill fragmentation and is not condoned by the manufacturers, the FDA, the surgeon general, CMS, the AMA, pharmaceutical malpractice insurers, and many others.

In fact, the California Medical Board did vote with the other medical boards [the National Association of Boards of Pharmacy (NABP) in Seattle in No. 97-4-01 voted on in 1998 – "Whereas, insurance companies and pharmacy benefit managers are advocating and mandating that practitioners prescribe and pharmacists dispense dosages of medications that may require the patient to physically split the medications … [programs that are] monetarily driven; therefore it be resolved that NABP oppose this mandate by working with] other national associations and government agencies to stop this potentially dangerous practice" [See Exhibit #2]

[5] Kaiser HMO, its hospitals, and the very profitable Permanente Medical Groups (the Federation) are run out of the Ordway building [pictured in Exhibit #3] – Mr. George Halverson and Dr. Francis Crosson being co-chairman of the top executive committee. They each have an office on the 27th floor – thus only a few doors down the hall from one another. They each hope to be aloof to these decisions that tie the hands of doctors at the frontline. Those physicians and pharmacisits who complain are deemed "not manage care suitable" and expelled. Many physicians don't even know that their prescriptions result in double doses and pill splitters – as a ER physician I did not catch on for one year. These decisions lead to the Sustainable Future of the partners – see the Permanente Map in the same Exhibit – not the patients. In fact, the unethical "group ethic" and the illegal "Permanente-patient relationship" are included on the greed map. This is "corporateering" at its worst.

[6] As the HMO Act of 1973 created federal enhancement of prepaid health plans like Kaiser (the mother or grandfather of HMOs), it also required "independent physician groups" be put at financial risk. Such IPAs – like the Permanente group – do take risk for profit but pass that risk on to patients as rationed and often dangerous care. The patient caries the risk of illness; the physician carries the likelihood of profit – million dollar plus pension plans creating $15,000 a month as the MDs turn senior.

[7] In fact, the topic should never be called "pill halving" [which rarely occurs] or even "pill splitting" [still sounds sort of even], but rather **pill fragmentation,** which is really what happens.

[8] The Kaiser lawyers are the first to point out that "Kaiser Permanente" does not exist as a legal entity. There are only three organizations who use a common strategy of care.

[9] I use the word funneling because Kaiser can achieve 98% uniformity of prescription for hypertension, diabetes, high cholesterol, etc. using the following tools: pocket reminders, EPIC program computer pop-ups, peer pressure, medication utilization tracking, pay check reminders, one on one talks, our-way-or-the-highway, etc. And the funneling is toward split pills – Tolinase, lisinopril, statin of the year, Paxil, Zoloft, Maxide, etc. The physician has little choice, so the patient has little choice. Pharmacists who complain are not encouraged to stay.

Time for Transparency

Transparency in health care is the only way to give back to seniors what has been so often stolen from them – the true information on which to base real consent. There can never be "informed consent" without the person being first fully informed.

And as this month is part of the-health-plan-switching period of time in Medicare, this is a good time for extra honesty. Either pill fragmenting is a way for the world to save $15 billion in pharmaceutical expense or a way to cost patients some $60 billion in early illness from uneven dosing.[10]

I originally sent you a formal complaint in 1998 - (#C1-98-17552). The silence of the previous Pharmacy Boards up until now – except for a quiet vote in Seattle [Exhibit #2] – has made the previous boards co-enablers of pill fragmenting in California. I ask that you transform your vote in Seattle to action in California. Further silence will simply endorse the status quo – massive pill splitting by the uniformed.

The Weighing Data

Is this "pill halving" or is it "pill fragmenting." The classic study of J.T. McDevitt in 1998 published in Pharmacotherapy [Exhibit #5] is quoted both by Kaiser and the VA as well as all experts on the topic of pill fragmenting. No one has ever proved him wrong. And these were volunteers from a newspaper ad, not sick patients.

Exactly 1752 pills were split by 94 healthy volunteers, the latter recruited from a newspaper ad. "Some 41.3% deviated from ideal weight by more than 10% and 12.4% deviated by more than 20%." Amazingly it did not matter if the pill had a score line or if the pill was split by hand or a pill splitter from Rite-Aid[11]. "Given the choice, 96.8% of volunteers stated that they would rather not split a tablet if a lower-dose formulation was available."

And what we find in the general practice of pill splitting is that dependent patients are compliant with the general funneling system toward one product. But they are uniformed of true risks. White coats give patients the impression that it is perfectly safe. The very labels used by the HMOs – Kaiser and United HealthCare[12] of the "Pill Halving" programs is 100% deceptive since halfs are not produced.

The VA has tried some weighing experiments even using a trained pharmacy student, and still the fragments were often greater than 10 percent of the hope for a half weight. In that study, the article suggested that lisinopril not be split; Kaiser does still split it. Those

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[10] Since most strokes are often sent home after Kaiser ER evaluation, the cost of care falls back to the family and not to the HMO.

[11] Rite Aid, Walmart, Walgreens, private pharmacists, Stanford, Harvard, Yale, etc. are not into pill fragmentation. It takes a dependent population who have prepaid benefits, a difficult path for legal suit, and the co-enabling by government - to pull of pill fragmentation.

[12] Dr. William W. McGuire who helped to okay pill splitting at United GroupHealth received an average compensation of $57,843,000 per year for his last six years.

VA areas with at least partial ethics had their patients split pills every other day – so big pieces would be matched with small pieces. They did not mention this in most of their articles; and Kaiser leans on VA "research" as its backup.

No one has done this weighing study with seniors who have the usual co-morbidities of arthritis, hypertension, high cholesterol, acid reflux, and occasional depression. This weighing experiment could be done easily and quickly.

Seniors can be on three Kaiser splits at one time – like Mary O'Donnell of Corcoran California who has now passed away. A page from her medication diary [Exhibit #6] and Kaiser medication records show the splitting of her blood pressure pill, her anti-cholesterol pill, and her anti-depression pill[13] all at the same time.

Or what about Audrey Timmis, an oxygen dependent patient who was asked to split Maxzide. Kaiser did not even order the smaller, senior dose for their formulary – regular dyazide (capsule) or Maxzide-25 – because the national goal in Kaiser pharmacy procurement in the Oakland highrise [See Exhibit #3] was to set up massive pill splitting and no choice. It saved money to order millions of Maxzide pills and have them rebundled into 100 pill bottles in Livermore. That translated for Audrey to have pieces – she called "tiddley winks" – flying all over her kitchen, even with her husband helping.[14] For goals spelled out in Kaiser-eeze in the Recovery Plan by 2001 – Audrey did not matter; profit mattered.

Kaiser's top profit year was 2004; the profit was $2 billion – half going to the physicians. And pill fragmenting contributed to the profit. That is blood money in my book. How many strokes and heart attacks we will never know – the evidence is swallowed. It is almost the perfect crime. But it lacks professional ethics. And that is why we have professional boards – to foster ethics and protect patients.

Am I Alone?

I am sometimes viewed as a Lone Ranger type in health care. However, my position against pill splitting is supported by:

1. the manufacturers [letter available from Merck];
2. the FDA safety committee;

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[13] **By the way, I was in Mary O'Donnel's house the day ABC News investigated pill splitting. She never felt she had Informed Consent or any choice. She was part of the law suit against Kaiser whereby after Kaiser's $1 million plus defense effort, the judges ruled that Kaiser was right – this issue belongs before the California Board of Pharmacy and the California Department of Managed Health Care. In fact, your ongoing "investigation" became their defense that they should not have to defend the same issue on more than one "front." They also admitted what I have long maintained, that "Kaiser Permanente" really does not exist. Kaiser maintains that they won this suit were embarrassed into dropping their splits from thirty-eight before the suit - including heart rhythm medication and seizure medication – down to about ten.**

[14] Another reliable patient has called these type of pieces "grenade fragments."

3. the American Society of Pharmacy Consultants – same policy for years;
4. most malpractice carriers for pharmacists;
5. increasingly seniors who start to understand pharmacy science;
6. veterans who wonder why the VA has never declared splitting safe by their Technical Advisory Committee;

Those who are against large splitting programs coming down from those who would be less responsible – like "Medical Directors" of HMOs – include:

1. the Surgeon General;
2. the FDA;
3. the National Boards of Pharmacy in Seattle;
4. the American Medical Association;
5. most of the physicians and pharmacists on the frontline of Kaiser who actually complement me privately for reducing the corporate pressure coming down from Oakland.[15]

Those who seem to like splitting include:

1. Top MDs and administrators at HMOs like Kaiser and United HealthCare with a focus on seniors (and great retirement programs for top management);
2. the VA regional programs who compete with each other for limited funds – really a federal HMO the same size as Kaiser;
3. "Pharmacy Benefit Managers" like those in Wisconsin and Michigan;
4. the "outcome centers" supported by the federal government and often a Kaiser Family endowed chair – like Stanford; though Stanford pharmacists have not joined this practice;
5. Medicaid wherever Pharmacy Boards are lax;
6. some newspapers who think that medications cost to much and do not have an independent pharmacist on staff to really explain the risk vs. benefit of uneven dosing;
7. pill splitter companies.

I admire those pharmacists in Kaiser who split the pills for the patients who need half pills because of no available size on the market – as in pediatrics. I do not admire those physicians and pharmacists who have decided to go along with this approach so as to achieve personal "vesting" goals for golden retirements. One group of future seniors should not get to the Golden Pond on the pain and suffering of other seniors.

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[15] One ex-Kaiser pharmacist might be willing to privately testify to a Board investigator. But the risk of going against Kaiser is to have one's career ruined. As with "The Firm," getting out of Kaiser without being damaged on the way out is very difficult. Those out of Kaiser can also be damaged by sympathetic IPAs and hospital "risk management" offices that can change alter medical records without a flit of conscience.

Kaiser would easily spend $5 million wining and dining all of the politicians possibly involved up through the Governor[16] to keep pill fragmentation programs humming along and to cast me as an outlier. Usually physicians like me are pictured as eagles soaring over the canyons of the past (like Dr. Welby) who had no real sense to know that it is either HMO medicine [called "private health plans"] or government medicine.

I hope to hear of the new investigations that this presentation should set off. But either way history will take note of what California allowed on each and every consumer board watch. And it will also conclude that a Board vote of each individual professional is as much a licensed decision as the handing over of a pill bottle [17] to a specific patient.

Conclusions

Of the two $35 billion a year budget organizations who split pills, the group over which you have authority to protect the public is Kaiser with 800,000 enrolled seniors[18] involved with Medicare D. As 75% of Kaiser has always been in California,[19] that is 600,000 vulnerable California seniors who will only learn about who "Thrives" when they get sick or need medication.

What is needed now by the Pharmacy Board is a rapid investigation that goes way beyond asking for another letter from Kaiser. It is time to show up unannounced at the frontlines of Kaiser care and to see what senior splits really look like. That means looking into the brown bags. Your eyes will tell you – as they did mine in 1998 – that there is no need to even have another weighing of fragments; this is really about pill destruction for high profit.

Too many many people are starting to call California "Kaiser-fornia." It is important that you do not let the tail wag the dog.

Don't take action for me. Do it for Maggie Dee, for Nick Feldman, and for the memory of Mary O'Donnell.

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[16] The style is for the Kaiser Plan to give the Permanente Physicians money that is then sent on to the governor. Or one of his pet projects is enhanced – like health care built on the magnification of HMOs.

[17] I briefly worked in a job with the Hmong community of Fresno that gave me only one choice for a medical plan – Kaiser. I joined so as to be a patient witness to what they do and what kind of misery it is to call into the system. They also managed to print one of my prescriptions in Spanish. I know Kaiser both as a former

[18] This may be found in the internal, 2006, year end summary written by Mr. George Halverson, CEO, Chairman of the Board, and President of the Kaiser Plan, Inc., and Kaiser Hospitals, Inc. – both using the same board. Identical boards allow money to travel down from the Plan to the for profit doctors and the for bonus hospitals and then travel back up through the hospitals to become bonuses at the top.

[19] Kaiser has withdrawn from many states in its history – New York, New Jersey, North Carolina, Texas, Missouri, Utah, etc – and has not ventured into a new state since developing its money losing plan in Washington, DC where it bought into Humana as the latter left. The Missouri Kaiser attempt folded because it had to send $4 million excess each year to prop up the DC unit – see court papers.

And do it for the Class of 2010 (see inside of your notebook); don't let them graduate into a world of challenged ethics. The Hippocratic Oath is both a Oath and a Covenant invoking upon anyone who would misuse these talents misery in this life and the next.

1 My CV and Textbook

2 NABP Resolution Against Large Scale Pill Splitting

3 Kaiser CEO + Top Physician – and the Permanente Map

4 California – 49% HMO Thrive Ads (Splitting Not mentioned)

5 McDevitt's Classic Study of Pill Fragmentation

6 Mary O'Donnel's Pill Diary – Three Splits at One Time

7 VA "SPOT" Harm Reports > 400

8 Nicholas Feldman and the Zanaflex fragments

1: Pharmacotherapy. 1998 Jan-Feb;18(1):193-7. Related Articles, Links

Accuracy of tablet splitting.

McDevitt JT, Gurst AH, Chen Y.

MEDEX Clinical Trial Services, Inc., Ardmore, Pennsylvania 19003, USA.

We attempted to determine the accuracy of manually splitting hydrochlorothiazide tablets. Ninety-four healthy volunteers each split ten 25-mg hydrochlorothiazide tablets, which were then weighed using an analytical balance. Demographics, grip and pinch strength, digit circumference, and tablet-splitting experience were documented. Subjects were also surveyed regarding their willingness to pay a premium for commercially available, lower-dose tablets. Of 1752 manually split tablet portions, 41.3% deviated from ideal weight by more than 10% and 12.4% deviated by more than 20%. Gender, age, education, and tablet-splitting experience were not predictive of variability. Most subjects (96.8%) stated a preference for commercially produced, lower-dose tablets, and 77.2% were willing to pay more for them. For drugs with steep dose-response curves or narrow therapeutic windows, the differences we recorded could be clinically relevant.

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Accuracy of Tablet Splitting

Joseph T. McDevitt, B.S., Andrea H. Gurst, B.S.N., and Yinshuo Chen, Ph.D.

We attempted to determine the accuracy of manually splitting hydrochlorothiazide tablets. Ninety-four healthy volunteers each split ten 25-mg hydrochlorothiazide tablets, which were then weighed using an analytical balance. Demographics, grip and pinch strength, digit circumference, and tablet-splitting experience were documented. Subjects were also surveyed regarding their willingness to pay a premium for commercially available, lower-dose tablets. Of 1752 manually split tablet portions, 41.3% deviated from ideal weight by more than 10% and 12.4% deviated by more than 20%. Gender, age, education, and tablet-splitting experience were not predictive of variability. Most subjects (96.8%) stated a preference for commercially produced, lower-dose tablets, and 77.2% were willing to pay more for them. For drugs with steep dose-response curves or narrow therapeutic windows, the differences we recorded could be clinically relevant.
(Pharmacotherapy 1998;18(1):193–197)

Tablet splitting is a frequent method of obtaining the prescribed dose of a drug. Physicians prescribe doses depending on a patient's disease and level of drug tolerance; however, drugs do not always come in the appropriate strength, in which case tablets must be broken into portions. When patients are instructed to split tablets that are not intended to be split, the potential for dosing errors is introduced.

It is a violation of pharmacy law in most states for a pharmacist to dispense split tablets. Recognition that dosing flexibility is required to treat patients accurately led certain pharmaceutical manufacturers to introduce tablets specifically intended for splitting (Glynase PresTab, Upjohn, Kalamazoo, MI; Tagamet TiltTab, SmithKline Beecham, Philadelphia, PA; etc.).

Relatively few controlled studies have been performed to evaluate the accuracy of splitting tablets. In one study, 10-mm oval tablets scored on both sides had the least variability in weight between portions when broken manually.[1] Large round tablets that were scored on one side tended to break unevenly, with large variability in weight between sides. Small (7-mm) round tablets were the most difficult to break accurately, with 44% of portions deviating from ideal weight by more than 20%. In addition, active drug was lost due to fragmentation and powdering during splitting. Some tablets have a protective coating that interferes with splitting, and others are specifically not intended to be split (e.g., enteric-coated tablets). Use of a tablet-splitting device resulted in findings similar to manual splitting.[2]

Currently, the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure recommends that the lowest effective dosage of a diuretic or β-blocker be first-line therapy for hypertension after a trial of lifestyle modifications.[3] Hydrochlorothiazide is frequently prescribed in this circumstance. A large body of evidence suggests that a low dosage (12.5 mg/day) is both effective and safe,[4–11] but dosages of 6.25 mg/day were not consistently effective in controlling hypertension.[12–14] At 12.5 mg/day, blood pressure reductions are generally similar to those with 25 mg/day, although with

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fewer metabolic adverse effects. Increasing the dosage beyond 50 mg/day generally does not improve blood pressure control.

Until recently, the agent was available only as a relatively small (6-mm diameter), 25-mg, round, scored tablet. It was therefore necessary to split the tablet to approximate a 12.5-mg dose. A 12.5-mg formulation of the agent (Microzide capsules; Watson Laboratories, Corona, CA) has been approved for marketing in the United States.

Methods

Ninety-four volunteers were recruited from a suburban Philadelphia neighborhood through a newspaper advertisement. Adult men and women were eligible to participate without regard to race, religion, or socioeconomic background. Subjects reporting severe vision impairment, missing arms or digits, or disabling arthritis were excluded. Demographic and survey information was collected from each volunteer (Table 1, Figure 1).

Table 1. Demographic Information

Variable	Mean (SD)	Range
Age (yrs)	42.6 (14.8)	20–77
Weight (kg)	74.38 (17.27)	45.4–136.2
M/F	39/55	
High school education (no.)	16	
College education (no.)	78	
Fingernail length	36 long, 58 short	
Tablet-splitting experience, yes/no (%)	35.1/64.9	

Measurements

Each subject's grip strength was measured using a hydraulic hand dynamometer (JAMAR, Jackson, MI) before splitting. The subject sat with arms resting on a table and palms facing medially. The dynamometer was set at level 1 with the indicator at zero. The subject was instructed to squeeze the dynamometer as hard as possible using one hand and a slow, steady grip. This procedure was repeated 3 times for each hand, and the subject's mean grip strength was calculated.

Pinch strength was documented using a standard pinch test gauge (B&L Engineering, Santa Fe Springs, CA). The subject sat at a table with arms pronated. The indicator on the pinch test gauge was set to zero. The gauge was placed between the subject's thumb and distal phalanx of the index finger. The subject slowly compressed the pinch tester, and the maximum value was recorded. This procedure was repeated 3 times for each hand, and the subject's mean pinch strength was calculated.

The circumferences of the distal phalanges of the right and left index fingers were measured using a standard ring gauge. The ring that slid on and off the fingers easily, but allowed no additional room, was judged to be the appropriate size. The size of the thumb of each hand just above the first joint was measured and documented using the same procedure. Finally, the length of the subject's fingernails was noted. Long and short fingernails were defined as those that did and did not extend beyond the digit, respectively.

Splitting Test

Each subject was provided with 10 tablets of hydrochlorothiazide (HydroDIURIL; Merck & Co., West Point, PA) that were randomly selected from a commercial supply bottle. Each tablet was weighed in milligrams on an electronic scale (Sartorius, Goettingen, Germany) before splitting. This scale had a minimum sensitivity of 0.001 mg. Subjects sat with forearms resting on a table and were instructed to split each of the tablets evenly by grasping and applying pressure to each side of the tablet with the thumbs and forefingers. If successful, subjects placed the tablet fragments from their right and left hands into appropriately marked containers, and the two portions were weighed in milligrams. This sequence was repeated until each subject had divided all 10 tablets.

In the event that a subject was unable to apply enough pressure to break a tablet manually, he or she was allowed to follow the same procedure using a commerical tablet splitter (Rite-Aid). Subjects who began splitting tablets manually but were unable to complete the process on all 10 tablets were allowed to divide the remaining tablets using the tablet splitter.

Statistical Analyses

Statistical tests of significance of preexisting conditions (age, gender, grip and finger pinch strength, finger size) on results of tablet splittin

1. Would you see a distinct benefit *not* to have to split tablets? (Yes/No)
2. Would you be willing to spend a little extra money for the convenience of not having to split tablets? (Yes/No
3. How much would you be willing to spend if a 1-month prescription originally cost $5, $10, $20, $50?

Figure 1. Survey.

Table 2. Results of Manual Tablet Splitting

	No.	Mean (SD)	Range
Whole tablet weight (mg)	876	108.6 (1.55)	104.0–114.0
Loss in splitting (mg)	1752	1.16 (1.78)	0–21.0
Loss in splitting (%)	1752	1.06 (1.63)	0–19.4
Tablet portion weight (mg)	1752	53.7 (7.26)	25.0–80.0
Variation of tablet portion from ideal*	1752	10.2 (8.7)	0–54.9

*Ideal weight 54.3 mg.

ere conducted with χ^2 tests for categoric data nd F test of analysis of variance for numerical ata. Calculations of descriptive statistics and all tatistical tests were conducted using SAS oftware (version 6.11).

Results

Ninety-four volunteers (55 women, 39 men) participated. A broad distribution of ages was represented: 34 volunteers were less than 35 years of age, 36 were age 35–44 years, and 24 were older than 55 years. All had completed high school and 83% had attended college. Most (85.1%) were right-handed and one was ambidextrous. Sixty-two percent of volunteers had long fingernails. Men had larger hands, on average, than women, as well as correspondingly stronger pinch and grip strengths. Slightly more than one-third of volunteers (35.1%) had experience splitting tablets.

A total of 876 tablets were manually split into 1752 portions and 51 were split into 102 portions with a commercial splitter (Table 2). The mean variation from ideal weight of manually split tablet portions was 10.9%, with approximately 1.1% of a tablet's weight being lost in splitting.

Slightly more than one-third of split tablet portions were within 5% of ideal weight; however, 41.3% deviated from ideal weight by more than 10%, 23.5% by more than 15%, and 12.4% by more than 20% (Figure 2). Similar results were found with the tablet splitter: 40.2% of portions were within 5% of ideal weight, and 37.3% deviated from ideal weight by more than 10%.

Analysis of variance (ANOVA) of the effect of gender, age, education, tablet-splitting experience, and presence of long fingernails failed to identify particular factor that predicted difficulty splitting tablets accurately. Firm grip strength in men was, however, inversely associated with the ability to split tablets accurately ($p=0.0001$). This factor was not identified as significant for women ($p=0.1569$). When failure to split a tablet within 15% or 20% of ideal weight was considered as an outcome, none of the demographic factors predicted failure; however, firm grip strength in men was identified by ANOVA to be significantly associated with increased failure at both the 15% and 20% levels. When drug lost in tablet splitting was measured, no patterns were identified that predicted increased loss, except that younger and older volunteers were slightly more likely to cause loss than middle-age volunteers (younger volunteers 1.22 mg lost, middle-age 0.86 mg lost, older 1.17 mg lost; $p=0.0082$, ANOVA).

Given the choice, 96.8% of volunteers stated that they would rather not split a tablet if a lower-dose formulation was available. Over three-fourths (77.2%) stated that they would be willing to pay more for a lower dosage strength, with the median amount being 20% over the original price of the prescription.

Discussion

Extensive analysis of the ability to split a 25-mg hydrochlorothiazide tablet accurately by 94 volunteers found that the average tablet portion

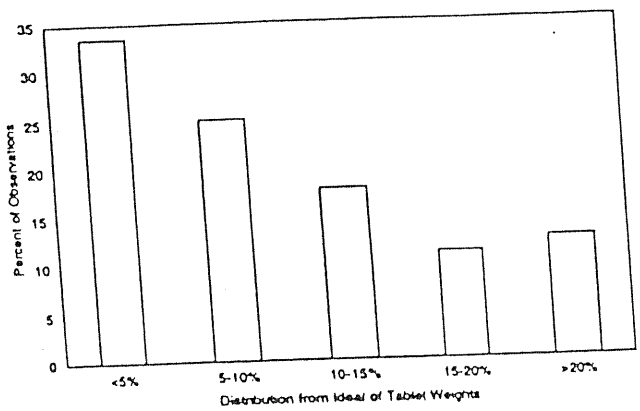

Figure 2. Distribution from ideal of manually split tablet portions.

varied from ideal weight by slightly greater than 10%, and that approximately 1.1% of the weight was lost in the splitting process. In addition, over 40% of portions deviated from ideal weight by greater than 10%, with almost 25% deviating by greater than 15% and over 12% by more than 20%. The use of a tablet splitter did not improve the accuracy of splitting.

Demographic and volunteer-specific data were captured to determine whether certain factors were predictive of inaccurate tablet splitting. Gender, age, education, and tablet-splitting experience were consistently found not to be predictive of accuracy. Only firm grip strength in men was a significant factor in predicting variation of tablet portion weight from ideal; grip strength was not predictive in women. No subpopulation existed that was consistently able to split tablets accurately. Thus, stereotypes regarding which patients might be "expected" to be able to perform this seemingly simple task should be discarded.

In rare circumstances (1.2%), the two tablet portions weighed more than the original whole tablet. This can best be explained by the transfer of finger oils from the subject to the tablet during splitting, and as a result, deviations from ideal may underestimate the true deviation from ideal. Such bias could be avoided with the use of unlubricated latex gloves, but that could have interfered with subjects' ability to split tablets accurately.

Several tablets were evaluated with respect to the percentage variation from ideal when split manually.[1] More than 87% of portions of oval 10-mm tablets with deep scores on both sides were within 10% of ideal weight. In contrast, smaller round tablets were more likely to yield inaccurate segment weights. Only 45% of round 8- or 9-mm tablet portions were within 10% of ideal weight, and 44% of round 7-mm tablet portions deviated from ideal by more than 20%.

The accuracy of a tablet-splitting device was assessed on 13 different agents available in tablet form.[2] The tablets differed in size, shape, and coating. Twenty tablets of each drug were split and the number of 40 resulting portions that were within 15% of ideal weight was determined. The best results were seen with larger tablets (> 600 mg) that were coated, and had an oblong (but not pointed) shape and flat edges. The smallest tablet tested was phenobarbital (4.1 mm, 30 mg), and this was among those with the highest percentage error.

Certain difficulties were observed with the tablet splitter, primarily with placing tablets in the correct position. Hazards associated with the device included potential injury due to the sharp steel blade attached to the lid, and the possibility of combining the present drug with powder or fragments of previously split ones.

As cost containment has become increasingly important, it is apparent that many physicians are responding by prescribing larger dosages of drugs and then instructing patients to split the tablets to receive the correct dose.[15] Some health maintenance organizations are providing tablet splitters to patients while dispensing larger than prescribed tablet sizes. Although this may be less expensive in the short run, it has not been proved to be financially or medically effective. Patients may be reluctant to split the tablets and decide to take double the dose at twice the dosing interval, thus leading to wide swings in blood concentrations. Alternatively, with polypharmacy common in many older patients, instructions regarding which drug to split may not be remembered between the time a prescription is received and the time the agent is taken, thus exposing the patient to unnecessary toxicity.

These results are applicable to other areas of therapy besides antihypertensives. In pediatrics, it is frequently necessary to split tablets, often into thirds or fourths. Although this was not the focus of the present study, it is reasonable to postulate that even greater errors would occur under these conditions. Because of the need to dose many drugs in children on a milligram per kilogram basis, these errors may be more important than in adults.

Our results may underestimate the variation from ideal in tablet portions. Tablets split by a patient in advance and returned to the pill bottle may be additionally subject to increased friability and fragmentation, hygroscopic absorption of water, and altered shelf life due to a break in the tablet's protective coating.

The *United States Pharmacopeia* specifies that a dosage formulation should be within ± 10% of its stated value. For most drugs, a variation of more than 10% probably would not influence therapeutic outcomes. Errors could be of concern for those with narrow therapeutic indexes (e.g., digoxin, warfarin), capacity-limited metabolism (e.g., phenytoin), or steep dose-response curves (e.g., hydrochlorothiazide).

Possible future areas of study could be a comparative bioequivalence trial of manually split tablets versus a commercially available formulation to determine if the accept

...nes for establishing bioequivalence are

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Medication
Diary of Kaiser
Patient -
Elderly and on Oxyge
- Three splits
at the same
time

MONDAY MAY 24, 1999

FLOVENT 3 2 PUFFS 2X DAY BID
COMBIVENT 3 PUFFS FOUR DAY
ZESTRIL 1/2 PILL
PRILOSEC 1 PILL
LASIX 1/2 PILL
METFORMIN 1 PILL
WELLBUTRIN 1/2 PILL

HHA 7:30-

TIPS

NCPS
VA National Center for Patient Safety

Volume 6, Issue 3 Topics In Patient Safety May/June 2006

Tablet Splitting

By Mariscelle M. Sales, Pharm.D., and Francesca E. Cunningham, Pharm.D.

Background

TABLET SPLITTING is a common practice often recommended by providers and implemented by healthcare systems. Splitting a tablet allows for a lower dose than that manufactured by the pharmaceutical industries, can facilitate administration of large tablets that patients may find difficult to swallow whole, and can give patients access to more expensive medications.

Tablet splitting has many benefits, and consideration of both drug and patient characteristics ensures safe and appropriate use.

Certain physicochemical properties of a drug influence the decision to split. For example, drugs with enteric coatings, extended-release formulations, and some combination products can cause adverse outcomes if split.[1-3]

In one study, elongated tablets scored deeply on both sides broke easily when manually split.[4] Tablet splitting devices were shown to perform best with larger tablets, tablets with flat edges, and oblong tablets without pointed ends.[5]

Drugs with narrow therapeutic windows should only be split if the physicochemical properties are adequate and if the optimal therapeutic response depends on the dose being halved. Also, patients with severe physical or visual impairments may hinder precision in pill splitting.

Tablets come in all shapes and sizes and require sharp instruments to divide them. Patients or their caregivers must have good vision, manual dexterity, and the mental capacity to accurately split a tablet. Accuracy of tablet splitting also depends on one's technique or device.

An optimal tablet-splitting device should have a hard, steel blade that goes all the way into the base when the lid is depressed. This will ensure a clean cut without leaving unusable fragments or crumbs that break off from the tablet. Additional benefits are provided when using a non-slip surface with adjustable grips to firmly hold the tablet steady and an optional magnifying attachment to enlarge the view of small tablets.

Any alteration of a medication may result in an adverse event or close call; hence, tablet splitting may cause problems in the medication use process. Using a good tablet-splitting device, unambiguous directions listed on the prescription, and identification/recognition of non-splittable medications comprise steps that can help to prevent problems from developing.

VA NCPS and the VA Center for Medication Safety Patient Safety Center of Inquiry (PSCI) embarked on an effort to evaluate potential medication problems caused by tablet splitting. Data on tablet-splitting events were evaluated using the NCPS Patient Safety Information System database (nicknamed "SPOT"). This article describes the results of that analysis.

Analyzing SPOT Data

Methods:

NCPS identified tablet splitting entries by querying the SPOT database for all RCA and safety reports involving tablet splitting from January 2001 to April 2005, forwarding the results to our Patient Safety Center of Inquiry for analysis. Search terms included: pill splitting, tablet splitting, half tablet, quarter tablet, ½ tab, and ¼ tab.

Data provided for each event included an anonymized case ID; date (year); free text description of event details; and record type (aggregate, safety report, RCA).

A complete evaluation of reports was conducted. Analysis of each individual case determined:

- Type of event (actual adverse event, close call, not enough information, or "other")
- Location of occurrence (inpatient or outpatient)
- Error type (overdose, underdose, incorrect directions, incorrect quantity, incorrect day supply, and incorrect strength dispensed)
- Medication characteristics (correct physicochemical properties, to include: non-extended release, no enteric coating and symmetric in shape; commercially available strengths; and high alert medications[6])
- Documented patient outcomes (no harm, minor harm, hospitalization, and/or permanent harm/death)

Results:

We found 442 reports in SPOT related to pill splitting. Below are selected, notable statistics from these events:

- 38% were adverse events
- 66% of the adverse events involved patients receiving more than their intended dose
- 65% of the adverse events occurred in outpatient settings
- 51% of the adverse events involved medications that came in commercially available strengths
- 28% of the medications were high alert
- 9% of the adverse events resulted in causing harm to a patient, but only 2% required hospitalization; no deaths were reported

Discussion

Limited literature suggests that manually or mechanically splitting tablets does not always produce equal portions.[7-15] The current evaluation of tablet splitting events within the VA revealed no problems regarding accuracy in splitting tablets to produce equal halves.

However, a potential source for problems was found in a number of areas: ordering, verifying, filling, and administering medications that require splitting.

continued on back page

Subj: **Re: questions about details of pill splitting**
Date: 1/28/2007 1:40:51 P.M. Pacific Standard Time
From: daretodream94704@yahoo.com
To: CPhil49401@aol.com

yes and here is my picture
CPhil49401@aol.com wrote:

> So you get to sleepy once a day and no relief once a day because they will not supply you with the 2mg tablet to take twice a day.
>
> In a message dated 1/27/2007 9:27:57 P.M. Pacific Standard Time, daretodream94704@yahoo.com writes:
>
> > The Baclofen did not work , It made me fall asleep .
> > You right about the 4mg . I was supposed to take it twice a day ,and now I take it just once.
> > thanks

Nicholas Feldman
Dare to Dream Attendant Services, LLC
275 5th St. #203
San Francisco, CA 94102
(800)988-9927
Fax: (415)541-8590
website: www.daretodreamattendantservices.com
blog: http://mydreamweaver.blogspot.com/
(Assistant may answer the phone)

Subj: **Re: questions about details of pill splting**
Date: 1/27/2007 9:27:57 P.M. Pacific Standard Time
From: daretodream94704@yahoo.com
To: cphil49401@aol.com

The Baclofen did not work , It made me fall asleep .
You right about the 4mg . I was supposed to take it twice a day ,and now I take it just once.
thanks

cphil49401@aol.com wrote:

> My pocket book of medications that I carry as an emergency physician states:
>
> "tizanidine (Zanflex): muscle spaticity due to MS or spinal cord injury: 4-8 mg PO q 6-8 pm, max 36 mg/d. [Generic/Trade: Tabs 2 & 4 mg, scored. Trade 6 mg.] $$$$"
>
> I'm thinking you are being asked to split the 4 mg. How often were you supposed to take it? Did you try Baclofen and compare? Dr. Phillips
>
> -----Original Message-----
> From: daretodream94704@yahoo.com
> To: cphil49401@aol.com
> Sent: Sat, 27 Jan 2007 4:21 PM
> Subject: Re: questions about details of pill splting
>
> 2.5 miligrams
>
> ***cphil49401@aol.com*** wrote:
>
> > Now I need the strength of the pill to verify that the half dose size was available as a full size pill either on the Kaiser formulary or to be bought. Dr. Phillips
> >
> > -----Original Message-----
> > From: daretodream94704@yahoo.com
> > To: CPhil49401@aol.com
> > Sent: Sat, 27 Jan 2007 2:04 PM
> > Subject: Re: questions about details of pill splting
> >
> > Dear Dr. Phillips,
> >
> > The answers are below in italics. I really hope this makes a difference, and that the pharmacy board really does something. We need more advocates like you.
> >
> > Thanks,
> > Nick Feldman
> >
> > ***CPhil49401@aol.com*** wrote:
> >
> > > 1. Tell me about your general health and whether you could be expected by dexterity to split pills. *I have cerebal palsy in all of my limbs. Kaiser wanted me to split my Zanaflex to help reduce my spasticity.*

2. Tell me if your physician explained that you would be asked to split pills or whether it happened at the pharmacy window. *The woman at the pharmacy counter very casually told me that I can split the pill to help spread it out longer.*

3. Tell me the name of the pill and how long the splitting lasted. *Zanaflex...indefinately*

4. Tell me if you gave up on splitting and simply take the whole dose every other day. *I gave up because I was not comfortable with my assistants having to split the pills. I also was never given a pill splitter, so determining what half the pill really is is really hard.*

5. Tell me if you have explained this to your physician or the pharmacist. Was any action taken? *Yes. No action was taken.*

6. Did you get any pill safety handout? *No*

7. Do you experience any side effects with the whole pill? *Yes. Drowsiness.*

8. Would you rather have the right does in a smaller pill? *Yes*

9. Can I share your answers with the California Board of Pharmacy and thus the public? *Yes*

10. Where do you live? Where do you get your care from Kaiser? *I live in downtown San Francisco, and I am seen at the Kaiser on Divisadero, and also at the French campus.*

Dr. Phillips

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blog: http://mydreamweaver.blogspot.com/
(Assistant may answer the phone)

Timolol [MC] *(Continued)*

vomiting, stomach discomfort, numbness in toes and fingers, dry sore eyes

Usual Dosage Children and Adults: Ophthalmic: Initial: 0.25% solution, instill 1 drop twice daily; increase to 0.5% solution if response not adequate; decrease to 1 drop/day if controlled; do not exceed 1 drop twice daily of 0.5% solution

Dosage Forms

Solution, as hemihydrate, ophthalmic (Betimol®) [$$$]: 0.25% (5 mL, 10 mL, 15 mL); 0.5% (5 mL, 10 mL, 15 mL)

Solution, as maleate ophthalmic (generic Timoptic®) [$$]: 0.25% (5 mL, 10 mL, 15 mL); 0.5% (5 mL, 10 mL, 15 mL)

Solution, as maleate, ophthalmic, preservative free, single use (Timoptic® OcuDose®) [$$$$$]: 0.25%, 0.5%

Recommended Alternative Levobunolol is the preferred ophthalmic beta-blocker

Generic Available No

- **Timoptic®** *see* Timolol [MC] *on page 743*
- **Tioguanine** *see* Thioguanine [MC] *on page 735*

Tiopronin

Brand Names Thiola™

Therapeutic Class 60:15 Resins & Chelating Agents

Use Prevention of kidney stone (cystine) formation in patients with severe homozygous cystinuria who have urinary cystine >500 mg/day who are resistant to treatment with high fluid intake, alkali, and diet modification, or who have had adverse reactions to penicillamine

Usual Dosage Adults: Initial dose is 800 mg/day, average dose is 1000 mg/day

Dosage Forms Tablet: 100 mg

Generic Available No

- **Tiotixene** *see* Thiothixene [MC] $$ *on page 739*
- **Tissue Plasminogen Activator, Recombinant** *see* Alteplase, Recombinant *on page 106*

Tizanidine $$$$$

Brand Names Zanaflex®

Synonyms Sirdalud®

Therapeutic Class 30:40.15 Skeletal Muscle Relaxants, Centrally-Acting Agents

Use Skeletal muscle relaxant used for the acute and intermittent management of increased muscle tone associated with spasticity

Contraindications Previous hypersensitivity to tizanidine

Warnings Reduce dose in patients with liver or renal disease; use with caution in patients with hypotension or cardiac disease. Use with caution in patients receiving antihypertensives. Do not use tizanidine in patients receiving alpha$_2$-adrenergic agonists.

Adverse Reactions

>10%: Hypotension, sedation, daytime drowsiness, somnolence, xerostomia

1% to 10%: Bradycardia, syncope, fatigue, dizziness, anxiety, nervousness, insomnia, pruritus, skin rash, nausea, vomiting, dyspepsia, constipation, diarrhea, elevation of liver enzymes, muscle weakness, tremor

<1%: Palpitations, ventricular extrasystoles, psychotic-like symptoms, visual hallucinations, delusions, hepatic failure

Kaiser

Drug Interactions

Oral contraceptives decrease tizanidine clearance.

Increased toxicity: Additive hypotensive effects may be seen with diuretics, other alpha adrenergic agonists, or antihypertensives; CNS depression with alcohol, baclofen or other CNS depressants

Usual Dosage

Adults: 2-4 mg 3 times/day

Usual initial dose: 4 mg, may increase by 2-4 mg as needed for satisfactory reduction of muscle tone every 6-8 hours to a maximum of three doses in any 24 hour period

Maximum dose: 36 mg/day

Renal/hepatic impairment: Reduce dosage

Monitoring Parameters Monitor liver function (aminotransferases) at baseline, 1, 3, 6 months and then periodically thereafter

Additional Information Tizanidine is a centrally-acting alpha$_2$-adrenergic agonist with dose-dependent effects and is pharmacologically similar to clonidine. Patients should be counseled regarding the possibility of hypotension after the first dose. During trials the reduction in blood pressure was seen within 1 hour after dosing, and peaked at 2-3 hours after the dose. At times the hypotension was associated with bradycardia, orthostatic hypotension, lightheadedness, dizziness, and syncope (rare). Clinical trial data suggests that tizanidine is not associated with muscle weakness like baclofen. However, this finding also did not lead to any consistent advantage as measured by activities of daily living. Data on the long-term administration of tizanidine are limited. No rebound hypertension was seen during clinical trials when tizanidine was tapered over 7 days.

Dosage Forms Tablet: 4 mg

Generic Available No

- **TNKase™** *see* Tenecteplase [FG] $$$$$ *on page 725*
- **TOBI™ Inhalation Solution [FR]** *see* Tobramycin [FR] [MC] *on page 745*

Tobramycin [FR] [MC]

Brand Names Nebcin® Injection; TOBI™ Inhalation Solution [FR]; Tobrex® Ophthalmic

Therapeutic Class 05:05.05 Aminoglycosides; 75:25.05 Anti-Infectives, Ophthalmic

Use Treatment of documented or suspected *Pseudomonas aeruginosa* infection; infection with a nonpseudomonal enteric bacillus which is more sensitive to tobramycin than gentamicin based on susceptibility tests; susceptible organisms in lower respiratory tract infections, CNS infections, intra-abdominal, skin, bone, and urinary tract infections; empiric therapy in cystic fibrosis and immunocompromised patients; topically used to treat superficial ophthalmic infections caused by susceptible bacteria

Restrictions *Formulary:* Tobramycin solution for inhalation (TOBI™) is restricted to prescribing CF Subspecialists, Pediatric and Adult Pulmonology

Pregnancy Risk Factor D

(Continued)

AT Journal
The Latest News & Resources in Assistive Technology
Vol. 97, May 15, 2004

A Personal Perspective...

By Nicholas W. Feldman

I can remember being 5 years old and my family all clustered around me, watching as I played my first video game using a chin control as I shot at the spaceships on the screen. It was 1980 and the Apple 2 + was all the rage. I had no idea what a significant role technology would play in my life as I grew up with Cerebral Palsy (CP).

Like a lot of children with CP, I went from school to school trying to find that, "equal education" that creates the integrated environment and allows the student with the disability to soar to their full potential. I sat in a special education kindergarten class where they told me about single input scanning. This is where you press a switch, using any part of the body (within reason) and it is connected to the CPU by a box. This then displays a row of letters, numbers, punctuation and a few very select groups of menu commands. The highlighted areas were divided into sections and if you pressed the switch in the right section, it would break down the individual letters, numbers and other symbols and when it would finally land on the right key, you would press the switch again and it would type it on the screen.

I am very verbal and my friend sitting next to me in that special education class was non-verbal and a lot was assumed for her. She was constantly told what to eat, what to wear, what to do and where she would go, via the request of our teacher to the classroom assistant. Then, one fine day, the teacher came to me and asked if I would empower my friend who was learning to do single input scanning, not on a computer per say, but a large board with different color lights with signs that said words like yes, no, bathroom, I want to eat, etc. My friend was very shy until that special board came along. The school had no idea what they were in for. Suddenly, questions that were once assumed now had different color lights and a whole personality to follow. I soon moved away and never really knew, but had a good imagination about my shy friend who, at age 6, finally got the opportunity to start making her own choices.

As I moved to different schools, with different levels of academic demand, I was still struggling with my single input scanning. I used a switch that was connected to a pillow on my headrest. I was doing this, but I had my sites set on bigger things like

being mobile with a power wheelchair. The technology had to allow me the ability to use my head to control a wheelchair. There was a company in Ohio, which had technology very similar to what I was using to activate the computer.
The wheelchair worked with a switch that was fastened to my headrest and when it was pushed, lights would flash on different arrows labeled "forward", "right", "left", "back" and all of the diagonal directions. To stop, the switch would need to be pushed again. By this time frame, it was the late 1980's and very early '90s. I was beginning to hear about not only portable computers, but I was fantasizing about sending an email to a friend in my car pool. Slowly, the Internet began to evolve and our family got its first subscription to an online service called Prodigy. I remember the first email I sent, was to my cousin who was serving in the military during the first invasion of Iraq.

Simultaneously, I was entering high school and was given a laptop computer and a new single input scanning system called words plus. This system had a feature called word prediction, which allows a slow type such as myself to have a list of possible words to choose from as you are typing. This vocabulary is primarily built by the words that it will remember after you type the word along with its own 68,000-word vocabulary. This made all the difference in the world especially when it came to book reports, essays, poetry, and letters that you weren't going to let your folks read.

The Internet was still in the first phase of the "web" and I was going into my junior year of high school. Someone with CP came down and demonstrated a voice activated program known as DragonDictate. This program, I had an opportunity to try out through a local computer access center which I was then affiliated with on an after school/volunteer basis. I became aware of some of the power in the Internet and through assistive technology such as the head master which has an infrared connection with a band that the user places around their forehead which emulates the mouse and a straw that the user uses to click and drag the mouse. There were now keyboards that would speak and new advancements in technology, which seemed to happen every millisecond.

I was just about to graduate from high school when I got a new type of wheelchair that had 3 switches that meant that with a new feature called "Cruise Control"; I could drive my wheelchair easier by pressing switches located on the sides of my headrest and one accelerator/brake. These features allowed me to drive and turn at the same time.

UC Berkeley was waiting for me with a big dose of Independent Living and much more of the Internet and disability culture. As I sit here speaking into my DragonDictate Classic controller along with a wheelchair, which I operate with my chin, I can function a lot more independently. I have worked with a lot of different access centers and independent living centers as well as the Department of Rehabilitation in order to fund all of this technology, which I had never dreamed of. I

even have a door opener that I can use with my headrest and a voice activated cell phone.

As an individual, my cerebral palsy has created some societal barriers, which the Internet breaks down. With a video camera and a microphone, everyone who I am in contact with is not always aware that I have a disability. Through all of my years, assistive technology has played an intricate role in so many areas of my life that includes: social (I, after 26 years, have a girlfriend, thank you messenger service), educational (typed and edited many college papers), housing (search through housing websites), and employment where I have had past jobs (dispatcher, independent living skills program coordinator, interim executive director of a non profit) and I currently work as the Oakland Center for Independent living as a Systems Change Advocate. As I go into the post education and job world, I continue to rely on assistive technology to help be my office for whatever opportunities await me. There is also the expectation that technology will continue to allow me the advancement and growth to continue affording me the opportunities that life with and without a disability has to offer and enjoy. I am hoping that the day will arrive when I say "get me up", a robot will be able to make my breakfast, program driving directions into my van, read me the latest email and news, walk my dog and vacuum the floor.

[AT JOURNAL | JOURNAL INDEX]

PRO Pill-Splitting

PRO

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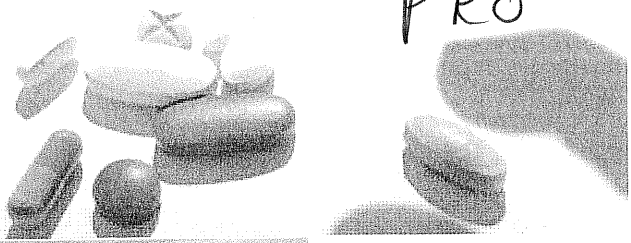
Free Guidance for Consumers on Prescription Medicines



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Selected Drug Reports

- Drugs for Heartburn, Acid Reflux Disease – PPIs
- Schizophrenia, Bipolar Disorder
- Overactive Bladder
- Sleeping Pills for Insomnia
- High Cholesterol, Heart Disease – Statins
- Asthma and Lung Disease – Inhaled Steroids
- Alzheimer's Disease Drugs
- Migraine Headache Drugs – Triptans
- Menopause – Female Hormones
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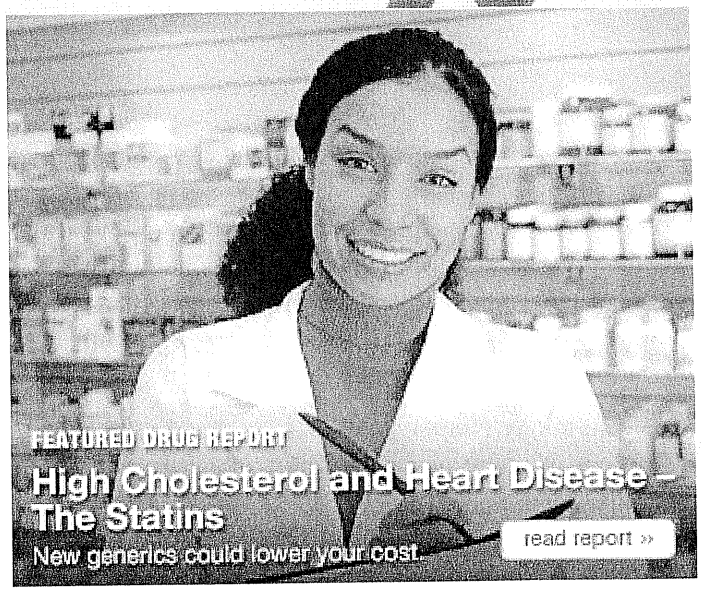
Full List >>



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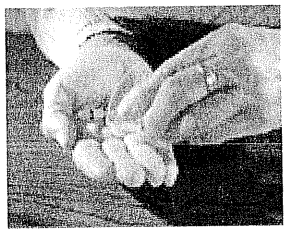

Pill-Splitting

It's safe and can save you lots of money

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SHOPPER'S GUIDE TO PRESCRIPTION DRUGS – NUMBER 1

Pill Splitting

If you take prescription drugs to treat a chronic illness, you could save money by splitting your pills – literally cutting them in half. Not all pills can be split, so pill splitting cannot be used in the treatment of every chronic disease. But in the face of mounting costs for prescription drugs, many doctors and health authorities are advising this strategy with more and more medicines. Most notably, all the cholesterol-lowering drugs known as statins can be split as can many of the drugs used to treat high blood pressure and depression.

Essentially, pill splitting allows you to buy two doses of medicine for the price of one – or get two months' worth of medicine for the price of one month. There is no danger in splitting pills as long as your doctor agrees that it's a good idea for you, you learn how to do it properly, and you split only pills that can be split. Simple pill splitting devices are now widely available.

BACKGROUND

Doctors have long counseled patients to split their pills. Initially, this was not to save money. Instead, it was to enable people to take a dose of medicine not readily available from a pharmacist. That's because drug companies make only a few fixed doses of any given medication. But many doctors prefer to tailor the dose of a medicine to a patient's exact needs, or to lower the risk of side effects. For example, a doctor may want to prescribe less of a drug (say, 10mg) than the lowest dose available (say, 20mg).

A common example of pill splitting these days involves good old aspirin. Health authorities now urge anyone at risk for heart disease to take half an adult aspirin tablet a day. A regular aspirin tablet contains 325mg, but studies show that 160mg or less is just as good at lowering the risk of a heart attack or stroke – and safer. Some companies now make half-dose aspirin tablets and children's aspirin comes in lower doses (generally 81mg). But often the least expensive alternative is to buy a large bottle of generic aspirin and split the pills in half.

Pill-splitting saves money because pharmaceutical companies and pharmacies often charge nearly the same amount for a particular medicine regardless of its dose. For example, a once-a-day drug may cost $100 for a month's supply of both a 100mg dose and a 50mg dose. Thus, if your doctor prescribes the 50mg pill, it'll cost you $100. But if he prescribes the 100mg pill and instructs you to cut it in half, $100 will buy you two months worth of medicine. If you take several medicines, that kind of savings can mount up.

Not surprisingly, many insurance companies are in favor of pill-splitting because it saves them money, too. Your employer may like the idea for the same reason. Some insurance companies now provide you with a list of approved drugs to split. And a few are even requiring pill-splitting by not covering the cost of some lower-dose drugs. This forces people to buy higher-dose pills and split them. The American Medical Association and the American Pharmacists Association oppose this practice. But these organizations acknowledge that many pills can be safely split if done correctly. The Department of Veteran's Affairs allows pill splitting at a number of VA facilities, though it does not formally endorse the practice.

Most drug companies oppose pill-splitting. They say it can be dangerous. But studies to date have not shown any adverse impact on health. In addition, by reducing the cost of prescription medicines, pill splitting could improve

SOME MEDICINES THAT CAN BE SAFELY SPLIT

- Amlodipine (Norvasc)
- Atenolol (Tenormin)
- Atorvastatin (Lipitor)
- Citalopram (Celexa)
- Clonazepam (Klonopin)
- Doxazosin (Cardura)
- Finasteride (Proscar)
- Levothyroxine (Synthroid)
- Lisinopril (Zestril)
- Lovastatin (Mevacor)
- Metformin (Glucophage)
- Metoprolol (Toprol)
- Nefazodone (Serzone)
- Olanzapine (Zyprexa)
- Paraxetine (Paxil)
- Pravastatin (Pravachol)
- Quinapril (Accupril)
- Rosuvastatin (Crestor)
- Sertraline (Zoloft)
- Sildenafil (Viagra)
- Simvastatin (Zocor)
- Tadafil (Cialis)
- Vardenafil (Levitra)

health outcomes by helping people afford the drugs they need and comply with the drug regimens their doctors recommend.

PRACTICAL ADVICE

Consult your doctor about pill splitting. The dose you take of most medicines is very important. If you don't get the right dose, the effect of the drug may be substantially reduced. Your doctor should know which drugs can be split and which cannot. You can consult a pharmacist, too, who may be willing to show you how to split your pills.

Pills are only safely split in half and never into smaller portions, such as into thirds or quarters.

There is no official, complete list of medicines that can be split, and some drugs are dangerous to split. That makes it doubly important to consult a doctor or pharmacist. Generally the following kinds of pills should *not* be split:

- Chemotherapy drugs
- Anti-seizure medicines
- Birth control pills
- Blood thinners (Coumadin, warfarin)
- Capsules of any kind that contain powders or gels
- Pills with a hard outside coating
- Pills designed to release the medication over time in your body
- Pills that are coated to protect your stomach
- Pills that provide drug release throughout the day
- Pills that crumble easily, irritate your mouth, taste bitter, or contain strong dyes that could stain your teeth and your mouth.

Examples of medicines that cannot be split include oxycodone (OxyContin) for pain, omeprazole (Prilosec) for heartburn, and cetirizine (Zyrtec) for allergies.

Some pills may deteriorate when exposed to air and moisture for long periods after being split. Therefore, you should not split your pills in advance. Instead, do it on the day you are taking the first half. Then take the remaining half on the second day.

Don't split your pills with a knife. This can be dangerous and generally is imprecise. That is, it leads to unequal halves too often, studies show. Instead, purchase a pill splitter. They cost from $3 to $10 and are available at most pharmacies and large discount stores. A device for splitting oddly shaped pills may cost more, up to $25. Some insurers will send you a pill splitter for free so check with your health plan.

If you have poor eyesight, or if you have an ailment like arthritis or Parkinson's disease, it might be difficult for you to split your pills. You should talk with your doctor about whether it might be too much of a burden. Likewise, people with memory problems or impaired thinking are not good candidates to split their pills.

The easiest pills to split are relatively flat round ones with a scored center. That's a slightly indented line that runs across the center of the pill. However, not every pill that has a scored center is meant to be split. Again, consult your doctor or pharmacist.

PILL SPLITTING SAVINGS – SOME EXAMPLES

Medicine and Daily Dose	Average Monthly Cost [1]	Potential Monthly Savings if Larger Dose Split in Half [2]	Resulting Average Monthly Cost with Split Pills
Lovastatin (Mevacor) 10mg	$33	$14.50	$18.50
Atorvastatin (Lipitor) 40mg	$124	$62.50	$61.50
Amlodipine (Norvasc) 5mg	$55	$18.50	$36.50
Sertraline (Zoloft) 50mg	$98	$49	$49
Metoprolol (Toprol XL) 200mg	$69	$9.50	$34.50

(1) Prices are nationwide retail averages; information derived by Consumer Reports Best Buy Drugs from data provided by Wolters Kluwer Health. (2) Dose used for calculation is double the dose listed in first column. Price of that dose is not given here.

THE SHOPPER'S GUIDE TO PRESCRIPTION DRUGS SERIES

This series is produced by Consumers Union and *Consumer Reports Best Buy Drugs*, a public information project supported by grants from the Engelberg Foundation and the National Library of Medicine of the National Institutes of Health. The project's free Web site is www.CRBestBuyDrugs.org.

PHARMACOECONOMICS

Tablet Splitting

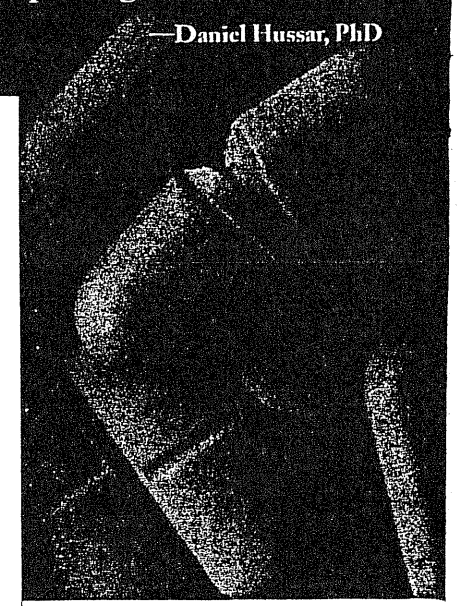
continued from page 16

Others view tablet splitting as a temporary escape from the larger issue of rising drug prices. "I'm glad that [Dr. Parra's] results were positive ... but it's not a solution, it's a Band-Aid," said Daniel Hussar, PhD, Remington Professor of Pharmacy, Philadelphia College of Pharmacy. "The issue that needs to be addressed full force is prices."

Even as a temporary solution, tablet splitting remain risky and underresearched, according to some. The American Society of Consultant Pharmacists' (ASCP) policy statement on mandatory tablet splitting (available at www.ascp.com/public/pr/policy/tabsplit.shtml) warns of forcing extra medication-handling procedures on patients with physical or mental limitations such as arthritis or parkinsonism. ASCP

'Who's saving the money [via tablet-splitting]? Is it the patient? The hospital? Pharmacists will spend more time talking to their patients but pharmacy benefits managers aren't going to agree to higher dispensing fees.'

—Daniel Hussar, PhD



Director of Policy and Advocacy Tom Clark, RPh, MHS, told *Pharmacy Practice News*, "Tablet splitting has been done clinically for many years, usually in cases where the patient needs a lower dose than is commercially available. But we don't want this to become widespread. Patients must be carefully selected and educated."

Both Dr. Hussar and Mr. Clark brought up practical questions involved in tablet-splitting programs. Considering long-term care facilities, Mr. Clark wondered whether already overextended nursing staff would be responsible for splitting tablets and where half-tablets would be stored. Having the pharmacist precut all tablets in a prescription poses its own problems, he noted. "Once a tablet's coating is breached, air and moisture can affect it. Is a half-tablet going to be stable for 30 days?"

Dr. Hussar raised issues regarding patient–pharmacist communications. "If the physician says one pill and the pharmacist says half a pill, who does the patient follow? What if the pharmacist splits the tablet and the patient thinks it still needs to be split?"

The bottom line on tablet splitting for Dr. Hussar remains the bottom line. "Who's saving the money? Is it the patient? The hospital? Pharmacists will spend more time talking to their patients but pharmacy benefits managers aren't going to agree to higher dispensing fees."

However, Dr. Parra noted a recent study showing that statins were the drug most likely to be discontinued by Medicare recipients because of cost. He added: "Although tablet splitting statins is not the solution for rising drug costs, it surely can have a role."

—Shayna B. Kravetz, BSc

Tablet Splitting

continued from page 1

Participation in the Florida program was voluntary. Tablet splitting eventually became the default for electronic orders of eligible prescriptions, although prescribers, patients or pharmacists could still opt for whole-tablet regimens. During 1999, 3,787 patients received daily doses of simvastatin at 5, 10, 20 or 40 mg. The patients were divided into two groups depending on whether they agreed to undergo voluntary conversion from whole simvastatin tablets to split tablets. Patients' low-density lipoprotein cholesterol (LDL-C) levels were followed through conversion to tablet splitting or, for patients who still received whole-tablet dosages, for at least 45 days.

With data for 1,098 patients in each group, 76.3% of patients in the tablet-splitting group achieved final LDL-C levels <130 mg/dL, versus 73.6% of those receiving whole tablets (P=0.14). The two groups also showed similar changes in LDL-C levels from baseline, and average final LDL-C values overall; patients in the tablet-splitting group averaged 110.9±29.6 mg/dL and patients who received whole tablets averaged 112.1±32.4 mg/dL (P=0.304). Patients' adherence to each regimen, as tracked by prescription refills, and transaminase levels did not differ significantly between the two groups.

The Pros and Cons

One benefit of tablet splitting is that some patients can save money. In a 2004 pilot program for Nebraska government employees, patients were offered $10 off each refill's copay if they split tablets for their prescriptions of sertraline (Zoloft, Pfizer), citalopram (Celexa, Forest), escitalopram (Lexapro, Forest), and atorvastatin (Lipitor, Pfizer). Participants received a tablet splitter and brochure directly from their health plan. In 2004's first quarter, 113 patients saved $2,360 and the state health plan saved $7,300, after paying administrative costs of $4,500, said Nina Homan, PharmD, Director of Pharmacy Programs, Prime Therapeutics, a pharmacy benefits solutions company based in Eagan, Minn.

see Tablet Splitting, page 18

To Split or Not To Split

The following suggestions for tablet splitting are based on an algorithm developed by the American Pharmacists Association Strategic Directions Committee (*J Am Pharm Assoc* 2004;44:324-325) and interviews with Daniel Hussar, PhD, Remington Professor of Pharmacy, Philadelphia College of Pharmacy, and David Parra, PharmD, Clinical Pharmacist, VA Medical Center, West Palm Beach, Fla.

The Prescription

Medications with narrow therapeutic indexes or unfavorable side-effect profiles are not suitable to tablet splitting. Capsules cannot be split, nor can tablets designed to have a sustained release or given enteric coatings to enable effective passage through the digestive system. Tablets should be able to withstand long-term exposure to air and moisture without degrading in texture or efficacy, especially if the pharmacist will split all tablets in advance.

The Patient

Physical limitations that may impede patients' ability to split tablets include lack of visual acuity or limited manual dexterity because of illnesses such as arthritis or parkinsonism and mental limitations such as Alzheimer's disease.

The Pharmacist

The pharmacist should take the following steps:

- Verify the relationship between the daily dosage prescribed and the dosage in the tablet as formulated;
- Ensure that both patient and prescription are suitable for a tablet-splitting program;
- Verify that the patient has a pill splitter and is educated on its use;
- Clarify with the patient what the prescriber has told him or her about the regimen and ensure that the patient receives a consistent message about how many doses to take each day; and
- Follow-up on delay in getting refills to promote patient adherence and to prevent the patient from mistakenly splitting presplit tablets.

finds. But pharmacists in the nation's more prevalent types of healthcare facilities, such as community and county hospitals, have been slower to advance into ambulatory clinical positions.

Results from the 2004 American Society of Health-System Pharmacists (ASHP) Survey of Ambulatory Care Pharmacy Practice in Health Systems, show that 233 of responding organizations Touro University—California in Vallejo, who led the ASHP research effort.

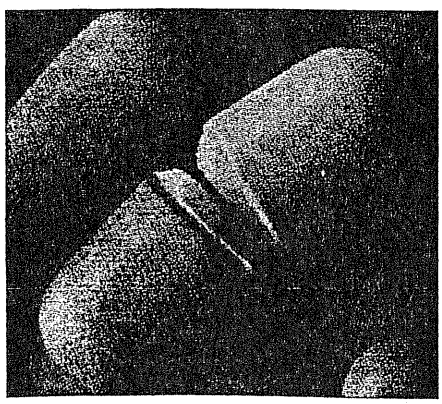
"If you're in a state or organization where your pharmacists are really stretched," said Dr. Knapp, "it's very difficult to take on new activities or expand into new areas when you're having trouble just keeping up with your traditional workload."

see Ambulatory Care, page 21

Tablet Splitting: Half A Solution to Drug Costs

Saving millions, but at a cost to patient care?

NEW ORLEANS—Splitting simvastatin tablets saved $1.26 million in 1999 at a Florida Department of Veterans Affairs (VA) network, with no loss in adherence or clinical outcomes, according to a retrospective analysis presented at the 2004 American Heart Association Scientific Sessions. Full implementation of the simvastatin-splitting initiative across the VA system nationwide avoided costs of $46.5 million in 2003, said lead researcher David Parra, PharmD, Clinical Pharmacist, VA Medical Center, West Palm Beach, Fla.



"[While] exploring ways to accommodate costs ... a number of VA hospitals had the same idea," said Dr. Parra. Simvastatin (Zocor, Merck) was chosen in part because prior research showed that statins could be administered in higher doses every second day and remain as effective as lower daily doses. "Simvastatin also has a very favorable dose-response profile and a good toxicity profile," he added. "If a patient splits a tablet 45/55 instead of 50/50, it won't matter."

see Tablet Splitting, page 16

ORIGINAL RESEARCH

Weight Uniformity of Split Tablets Required by a Veterans Affairs Policy

JAMES E. POLLI, PhD; SHARON KIM, BA; and BRIAN R. MARTIN, PharmD

ABSTRACT

OBJECTIVE: To split several tablet products relevant to the Veterans Affairs (VA) Maryland Healthcare System and assess whether the resulting half tablets provide equal doses.

METHODS: From a VA list of products that are required to be split, 7 products were evaluated, along with 5 other commonly split tablet products. A trained pharmacy student split tablets using a tablet splitter provided by the VA. Half tablets were assessed for weight uniformity.

RESULTS: Of the 12 products subjected to splitting, 8 products (atorvastatin, citalopram, furosemide, glipizide, metoprolol, paroxetine, sertraline, and warfarin) yielded half tablets that passed the weight-uniformity test. The 4 failing products were lisinopril, lovastatin, rofecoxib, and simvastatin. Unusual tablet shape and high tablet hardness predisposed products to failing the weight-uniformity test. The 4 failing products resulted in half tablets that were generally within 20% of their target weight range, suggesting that splitting these specific products would not result in adverse therapeutic effects due to dose variation created by tablet-splitting.

CONCLUSION: Split-tablet results were relatively favorable and generally support a VA practice to split specific tablets. Public quality standards for half tablets, including their content uniformity, are needed to better delineate the policies for acceptable tablet splitting.

KEYWORDS: Tablet splitting, Weight uniformity, Tablet-weight uniformity, Veterans Affairs

J Managed Care Pharm. 2003;9(5):401-07

Authors

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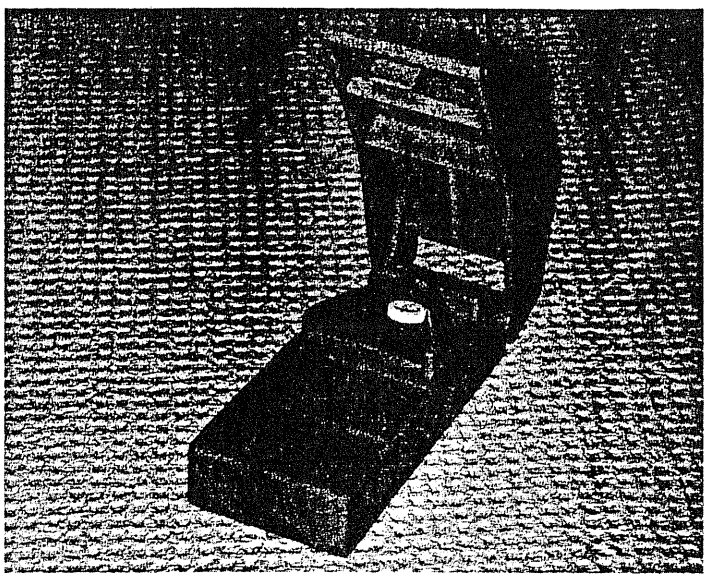
In recent years, the U.S. Department of Veterans Affairs (VA) has been faced with escalating pharmacy costs. These increased costs are the result of increased enrollment, an aging patient population that requires more prescription medicines, and increased acquisition costs of prescription medicines. The VA has turned to tablet-splitting programs as one approach to contain costs. Several pharmacoeconomic studies have indicated that splitting certain tablets can produce significant cost savings.[1-5]

A tablet-splitting program was implemented 2 years ago at the VA Maryland Health Care System, which is part of the Veterans Integrated Service Network 5 (VISN 5) region. VISN 5 provides care for veterans in Maryland; Washington, D.C; eastern West Virginia; Northern Virginia; and south central Pennsylvania.

Candidate drugs were considered for this tablet-splitting initiative if they had a relatively high cost, tablet splitting was not considered to be detrimental to drug release, and the tablets were easily split with a standard tablet-splitting device. VISN 5 now mandates tablet splitting of 8 tablet products for outpatients: atorvastatin, citalopram, lovastatin, paroxetine, rofecoxib, sertraline, sildenafil, and simvastatin. New prescriptions for these products are filled with a tablet that contains twice the prescribed dose, and patients are instructed to take 1 half tablet. A standard tablet-splitting device is also dispensed with the prescriptions. A patient may opt out of the tablet-splitting program if the splitting of tablets proves to be difficult. Also, several other tablets are frequently split, due to cost and therapeutic reasons. Between May 2001 and April 2002, the tablet-splitting initiative directly saved the VA Maryland Healthcare System about $560,000; approximately 41,000 patients received pharmacy services from the health care system during this time.

Equal splitting is presumably necessary for weight uniformity from half tablet to half tablet. We previously found that several commonly split tablets, when split by a razor blade or by hand, usually did not produce evenly split tablet halves.[6] We observed that no visible tablet features (e.g., tablet scoring) predisposed a product's half tablets from passing or failing the uniformity test. Rosenberg et al. found tablet splitting to yield half tablets that generally did not meet an expectation for dose uniformity.[7] They determined the weights and weight uniformity of tablet halves dispensed by pharmacists. Rosenberg et al. found that only 7 of the 22 dispensed prescriptions met an expectation of accurate tablet halves (defined as less than 15% error) with acceptable weight uniformity (i.e., less than 6% relative standard deviation).

FIGURE 1 Photograph of Tablet Splitter



From these recent studies, we hypothesized that tablet splitting following practices of the VA Maryland Health Care System would result in half tablets that generally fail to provide acceptable dose uniformity. Specifically, the objective of our study was to split several tablet products relevant to the VA Maryland Healthcare System and assess whether the resulting half tablets provided equal weights. Seven of the 8 mandatory split products in the VISN 5 region (all but sildenafil) were evaluated, along with furosemide, glipizide, lisinopril, metoprolol, and warfarin, which are commonly split at the VA Maryland Healthcare System. Although not mandatory, splitting of these latter 5 products is permissible, at the discretion of the prescriber. Splitting tablets allows for more precise dosage adjustment and greater patient convenience, for example, by eliminating the need for 2 separate prescriptions to achieve a desired dose. For instance, a patient prescribed lisinopril 30 mg daily can take a 20 mg and a 10 mg tablet, which would require 2 copayments since a 30 mg tablet is not commercially available. Alternatively, the patient could be prescribed one and one-half 20 mg tablets daily, which requires only 1 prescription and only 1 copayment.

Methods

The following products were donated by either the VA Maryland Healthcare System or the University of Maryland School of Pharmacy: atorvastatin 40 mg (Lipitor, Pfizer, Lot #053X0V), citalopram 40 mg (Celexa, Forest, Lot #M0114M), furosemide 40 mg (Geneva, Lot #114028), glipizide 10 mg (Geneva, Lot #126255), lisinopril 40mg (Prinivil, Merck, Lot #L4686; generic lisinopril was not available at the time of this study but is now purchased by the VA), lovastatin 40 mg (Mevacor, Merck, Lot #L1143; generic lovastatin was not available at the time of this study but is now purchased by the VA), metoprolol tartrate 50 mg (Caraco, Lot #1333A), paroxetine (Paxil, GlaxoSmithKline, Lot #400019B13), rofecoxib 25 mg (Vioxx, Merck, Lot #L3103), sertraline 100 mg (Zoloft, Pfizer, Lot #9JP018A), simvastatin 20 mg (Zocor, Merck, Lot #L1016), and warfarin 5 mg (Coumadin, DuPont Pharmaceuticals, Lot #SP094A).

The previously described tablet-splitting method and acceptance criteria were followed,[6] with the exception that a tablet splitter (ACE-LIFE Pill Splitter model PS12E; Health Enterprises Inc., North Attleboro, MA) was used. This tablet splitter consists of upper and lower platforms, which are connected by a hinge. The lower platform provides for the placement of the tablet within a V-shaped region. A razor blade is centered on the upper platform. A tablet is split by pressing the upper platform onto the lower platform (Figure 1). This model of tablet splitter is distributed to VA patients who are instructed to split tablets. For this study, one trained, supervised pharmacy student (tester) performed all tablet splitting in a controlled laboratory environment. This study design did not employ patients; rather, it employed a trained tester to split tablets, since individual patients are known to vary in their ability to split tablets. In evaluating the hypothesis that tablet splitting would result in half tablets that generally fail to provide acceptable dose uniformity, our methodology represents a best-case approach.

Each tablet was carefully placed in the designed split area of the splitter; in all cases, the aim was to obtain evenly split tablet halves. The tester split Zestril 40 mg tablets to affirm the ability of the tester to obtain the favorable tablet-splitting results reported previously (i.e., weight uniformity that passes the acceptance criteria).[6] If a tablet was scored, the tablet was situated in the splitter such that the blade would cut within the score groove. However, for warfarin and furosemide, splits were also performed when the tablet was randomly placed in the splitter (i.e., random orientation of the tablet score relative to the blade). Also, because of its trapezoid shape, lisinopril (Prinivil) could be placed into the splitter with 2 different orientations; both orientations were evaluated.

The previously applied criteria were followed in assessing whether the resulting half tablets split uniformly.[6] The criteria were adapted from the U.S. Pharmacopeia's (USP) <905> "Uniformity of Dosage Units" test for whole tablets.[8] Briefly, the test entailed subjecting 30 tablets of each product to the following:

- 30 tablets were weighed. The mean weight per tablet was calculated. The acceptable 85% to 115% range for a perfectly split tablet was determined from this mean weight. All weight measures employed a Mettler AE 100 analytical balance (Mettler Toledo, Inc., Columbus, OH).
- 10 of the 30 tablets were individually weighed. Each tablet was split, resulting in 20 half tablets. Each half tablet was weighed.
- From the 20 half tablets, the number of tablet halves outside the 85% to 115% range was counted. The number outside the 75% to 125% range was also counted. The relative standard

TABLE 1 Performance of Tablets That Split Successfully

Product	Percent Outliers Beyond 85%-115% (and Beyond 75%-125%)	Percent RSD	Percent Dose Loss (≤ Max)	Observations	Scored (Y/N)	Flat (Y/N)	Tablet Shape
Celexa 40 mg	0 (0)	6.1	0.2 (0.4)	Dramatic score; appears to facilitate accurate splitting	Yes	No	Oval
Coumadin 5 mg (orientation 1)	0 (0)	3.3	0.00 (0.18)	Tablet situated such that blade would split tablet along the score	Yes	No	Round
Coumadin 5 mg (orientation 2)	0 (0)	6.2	0.5 (1.4)	Tablet situated such that score was randomly oriented relative to blade	Yes	No	Round
Furosemide 40 mg (orientation 1)	0 (0)	3.9	0.8 (1.7)	Tablet situated such that blade would split tablet along the score	Yes	Yes	Round
Furosemide 40 mg (orientation 2)	0 (0)	7.8	1.3 (7.3)	Tablet situated such that score was randomly oriented relative to blade	Yes	Yes	Round
Glipizide 10 mg	0 (0)	6.1	0.08 (0.95)	Tablet situated such that blade would split tablet along the score	Yes	No	Round
Lipitor 40 mg	0 (0)	5.5	0.1 (0.4)	Tablet situated such that blade would split tablet where a score would be; difficult to position in the splitter	No	No	Oval
Metoprolol 50 mg	0 (0)	5.4	0.1 (0.4)	Tablet situated such that blade would split tablet along the score but the most difficult to position in the splitter since the tablet is oblong	Yes	No	Oblong
Paxil 40 mg	0 (0)	3.5	0.56 (1.00)	Tablet situated such that blade would split tablet where a score would be	No	No	Oval
Zoloft 100 mg	0 (0)	3.3	0.1 (0.3)	Tablet situated such that blade would split tablet along the score	Yes	No	Oblong

deviation (RSD) of the half-tablet weights was calculated. If, at most, 1 half tablet was outside the 85% to 115% range, but within the 75% to 125% range, and if the RSD was ≤10.0%, the half tablets passed this uniformity test.

- If 2 half tablets were outside the 85% to 115% range (but within 75% to 125% range) or if RSD >10.0%, the additional 20 tablets were split. To pass, none of the additional 40 half tablets could be outside the 85% to 115% range, and the RSD for all 60 half tablets needed to be ≤10.0%.
- If 3 or more of the 20 half tablets were outside the 85% to 15% range, the half tablets failed this uniform test. Also, if any half tablets were outside the 75% to 125% range, the half tablets failed this uniformity test.

Hence, like the USP "Uniformity of Dosage Units" test for whole tablets, half tablets could fail because of too many half tablets outside the 85% to 115% range, too many half tablets outside the 75% to 125% range, or too high an RSD. However, the criteria applied here are more liberal than the USP test for whole tablets, since the USP test allows an RSD of a maximum 6%. Also, half-tablet weight, rather than chemical assay of actual drug, was evaluated. These 2 aspects facilitate tablet halves to pass the uniformity test. The percent-dose loss due to the splitting process was also monitored. The percent-dose loss was the relative difference between the weight of the original tablet and the combined weight of its 2 half tablets.

Results

Of the 12 products subjected to splitting, 8 products (67%) yielded half tablets that passed the weight uniformity test. These results generally contrast with previous results where 8 of 11 razor-blade-split products provided half tablets that failed.[6] Tables 1 and 2 list the products that passed and failed, respectively. Using a tablet splitter in this study, all 6 scored tablets passed, while most unscored tablets failed (4 of 6 failed). This tendency conflicts with a previous observation that no visible tablet features (e.g., tablet scoring, tablet shape) predisposed a product's half tablets from passing or failing the uniformity test.[6] Among the 3 products included in both our previous and the present study, paroxetine and sertraline each passed in both studies, while atorvastatin failed previously but passed here.

Warfarin and furosemide passed, regardless of how the tablet score was oriented relative to the splitter's blade (Table 1). For each of these products, results from the random orientation were slightly less desirable than the results from the nonrandom orientation. Lisinopril failed, regardless of how the tablet score was oriented relative to the splitter's blade (Table 2).

Rofecoxib and simvastatin (Table 2) failed the uniformity test for every reason: too many half tablets outside the 85% to 115% range, too many half tablets outside the 75% to 125% range, and too high an RSD. Lovastatin and lisinopril in one orientation (i.e., the orientation that provided a more stable fit of the Prinivil tablet within the tablet splitter) failed for 2 of these 3 reasons. Lisinopril in the other orientation (i.e., the orientation that provided a poor fit of the tablet within the tablet splitter) failed for all 3 reasons.

Discussion

Favorable Tablet-Split Results

The objective of this report was to split several tablet products relevant to the VA Maryland Healthcare System and assess

TABLE 2 Performance of Tablets That Did Not Split Successfully

Product	Percent Outliers Beyond 85%-115% (and Beyond 75%-125%)	Percent RSD	Percent Dose Loss (≤ Max)	Observations	Scored (Y/N)	Flat (Y/N)	Tablet Shape
Mevacor 40 mg	15 (0)	10.4	0.9 (3.2)	Failed by a small margin	No	Yes	Octagon; thick
Prinivil 40 mg (orientation 1)	20 (0)	13.4	1.5 (7.2)	This orientation provided a good fit of the tablet within the tablet splitter	No	Yes	Trapezoid (but not a square); top of the tablet was inserted toward the blade of the tablet splitter
Prinivil 40 mg (orientation 2)	40 (10)	15.8	0.6 (1.0)	This orientation provided a poor fit of the tablet within the tablet splitter	No	Yes	Trapezoid (but not a square); bottom corner of the tablet was inserted toward the blade of the tablet splitter
Vioxx 25 mg	50 (20)	21.1	1.9 (6.2)	Thick and hard tablet; most difficult to split since the blade is able to move tablet during splitting	No	No	Round; the tablet is almost spherical, due to its small tablet diameter, round shape, and convex (nonflat) surface
Zocor 20 mg	20 (10)	15.0	0.00 (1.30)	Difficult to position the tablet in the splitter	No	No	Shield-like; the tablet's sharpest point was inserted toward the blade of the tablet splitter

whether the resulting half tablets provided equal doses. Our findings here are surprisingly favorable. Using the same criteria applied here, our previous observations from razor-blade splitting showed that a majority of tablets did not split evenly and visible tablet features did not predict a product's half tablets from passing or failing the uniformity test.[6] Using similar criteria, Rosenberg et al. also observed tablet splitting that resulted in half tablets that generally did not exhibit half-tablet uniformity.[7]

Hence, our expectations for this study were low. However, the results are relatively favorable and generally support the mandatory tablet-split policy of the VISN 5 region. Of the 12 products subjected to splitting, 8 products yielded half tablets that passed the weight-uniformity test. For these 8 products, including warfarin, it would appear that motivated and capable patients, under the direction of a pharmacist, would not experience any adverse therapeutic effects due to dose variation from tablet splitting. This conclusion is based on the half tablets of these 8 products exhibiting weight uniformity to whole tablets.

One possible explanation for the differences between this study, where a majority of tablets passed, and our previous results, where a majority of tablets failed, is that the use of a specific model of tablet splitter provided better tablet splitting. However, Sedrati et al. identified several tablet products that, when split using a tablet splitter, resulted in half tablets with doses outside a 85% to 115% range of the target half-tablet dose.[9] Similarly, Horn et al. found several products used in pediatric patients to not split equally.[10] Another possibility is that the VA was selective in identifying tablet products for splitting (i.e., preferentially selected tablets that split evenly). The VA has previously indicated that sertraline tablets split accurately.[11]

Possible Role of Tablet Shape and Hardness in Less-Favorable Tablet-Split Results

The 4 products that failed the weight-uniformity standard were lovastatin, lisinopril, rofecoxib, and simvastatin. In contrast to our previous observations that scoring, or any other visible characteristic, could not predict uniformity test results,[6] a tablet score here tended to explain whether a tablet passed or failed the uniformity test. However, we suspect that shape and tablet hardness, and not scoring, were perhaps the true determinants of acceptable uniformity. Relative to the products that split evenly (Table 1), 3 of the 4 failed products (Table 2) have unusual shapes. Lisinopril (Prinivil) is trapezoidal in shape, with no central axis that could provide an even split. Additionally, lisinopril, in either orientation, did not sit well within the tablet splitter; the tablet did not match the angle of the tablet splitter and rocked as the blade cut through the tablet, particularly for the second orientation (Table 2). Simvastatin's positioning within the splitter was unstable because of the tablet's shield shape. In contrast to the unusual shapes of lisinopril and simvastatin, the roundness of glipizide facilitated its favorable positioning within the tablet splitter.

The hardness and spherical shape of rofecoxib resulted in difficult, unreliable splitting. (Tablet hardness was assessed by the tester's perception of the force required to split the tablets; rofecoxib tablets were deemed the hardest tablets.) Rofecoxib's extreme hardness required that the tablet-splitter's blade be firmly pressed into the tablet. Subsequently, this great force caused the tablet to uncontrollably rock as the tablet was cut. Rofecoxib also lost the most tablet residue (i.e., "crumbs"), because of the need to press hard on the tablet splitter.

Lovastatin did not exhibit any apparent shape or hardness difficulties, but it marginally failed. Lovastatin is a relatively thick tablet for its small size.

Interestingly, all 4 products from Merck failed, and all non-Merck products passed. These Merck products—lisinopril, lovastatin, rofecoxib, and simvastatin—do not appear to share any one common physical characteristic, except that each has an unusual shape to some extent.

Lovstatin and Lisinopril: Clinical Considerations

For lovastatin, 15% of the half tablets exhibited weights greater than ±15% of target. For one orientation of lisinopril within the tablet splitter (i.e., orientation 1, where the top of this trapezoidal-shaped tablet was placed toward the splitter's blade), 20% of the half tablets exhibited weights greater than ±15% of target. The percent RSD for lovastatin and lisinopril half-tablet weights was just over 10%. A similar degree of failure was previously observed with several other products.[6] Cohen has indicated that this degree in half-tablet weight variability is acceptable since therapeutic outcomes would likely be unchanged.[5]

Given the wide therapeutic index of lovastatin[12,13] and lisinopril,[14] it would appear that splitting these 2 products is acceptable. Gee at al. found that splitting HMG Co-A reductase inhibitors such as lovastatin had no negative effect on lipid panels or liver enzyme tests.[15] Laboratory lipid and liver enzyme tests were conducted before and after 512 patients were enrolled in an HMG Co-A reductase inhibitor tablet-splitting program. Among the patients, 85% of the patients were treated with simvastatin, 15% were taking lovastatin, and 1 patient was administered atorvastatin. Patients were maintained on the same HMG Co-A reductase inhibitor and dose before and after implementation of the program. Laboratory results comparing whole- and half-tablet performance from all 512 patients indicated that there was no change in total cholesterol and triglycerides. Statistically, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) changed favorably, and liver enzymes AST and ALT each increased, although these changes were apparently not clinically significant. These results suggest that a split-tablet program had no effect of HMG (e.g., lovastatin) clinical outcomes.

Rindone found that splitting lisinopril did not change control of stable hypertension.[16] Rindone randomized 28 patients with hypertension, who were on stable doses of lisinopril, into a crossover clinical trial. Patient blood pressures were measured when they were taking whole tablets and split tablets. No statistically significant differences in systolic or diastolic blood pressures were observed between whole-tablet and split-tablet groups.

Simvastatin: Clinical Considerations

Relative to lovastatin and lisinopril, tablet-splitting results for simvastatin were less satisfactory (Table 2). Twenty percent of the half tablets fell outside the ±15% target weight range, with half of those half tablets falling outside the ±25% target weight range. However, 3 studies have assessed the clinical performance of split simvastatin tablets and found favorable results. Using retrospective chart review, Duncan et al. evaluated the effect of splitting simvastatin on patient LDL cholesterol and total cholesterol.[17] Patients were taking simvastatin whole tablets and obtained regular lipid management and cholesterol measurements. Patients were converted to split tablets and maintained the same milligram-per-day dose. There was no statistically significant increase in either LDL or total cholesterol after conversion to split tablets; in fact, each laboratory value decreased. Duncan et al. conclude that half-tablet dosing of simvastatin was as effective as whole-tablet dosing. They also found similar findings for atorvastatin.

In a similar study, Rindone and Arriola converted hyperlipidemic patients from fluvastatin to simvastatin, where patients were instructed to use a tablet splitter to split simvastatin tablets in half.[18] In the 56 patients who completed the study, total cholesterol, triglycerides, and high-density lipoprotein were unchanged, with LDL statistically decreasing. Rindone and Arriola indicate that this substantial cost-savings approach, which, in part, relied on splitting simvastatin tablets, exhibited lipid control in the majority of patients. Most recently, Gee et al. measured laboratory lipids and liver enzyme levels in 512 patients who were enrolled in a HMG Co-A reductase inhibitor tablet-splitting program, where 85% of the patients were treated with simvastatin, as described above.[15] These 3 studies, along with the present split-tablet results and wide therapeutic index of simvastatin,[19] support the mandatory tablet-split policy for simvastatin.

Rofecoxib and Sildenafil: Clinical Considerations

Rofecoxib tablets provided the least desirable half tablets. Fifty percent of the half tablets fell outside the ±15% target weight range, 40% of those half tablets fell outside the ±25% target weight range. Since refocoxib has a high therapeutic index,[20,21] we anticipate that these rofecoxib dose variations will not result in adverse clinical outcomes. The effective daily dose of rofecoxib ranges from 12.5 mg to 50 mg, but the drug is not particularly sensitive to dose. Further, when healthy volunteers were administered up to 5 times the maximum recommended dose for a period of 14 days, no serious toxicities were observed[21]; hence, dose variations from rofecoxib half tablets do not present a toxicity problem.

While sildenafil tablets were not split here and are on the VISN 5 mandatory split list, a clinical study supporting VA policy by Orrico et al. found that the dose of sildenafil citrate could be titrated to the lowest effective dose while incorporating tablet splitting as a method to reduce drug cost.[22] In 96 patients, 58% responded to 50 mg (half tablet) of the drug.

Further Managed Care Considerations

To date, the mandatory tablet-splitting program continues to

offer a substantial costs savings to the VA, both on a local and a national level. Results here support this program, as weight uniformity was generally acceptable for these products. Tablet-splitting initiatives offer the VA, and potentially other managed care organizations, an attractive cost benefit, while maintaining quality health care for health plan members.

As demonstrated here with the several nonmandatory split products tested, other prescription medications may be suitable for a tablet splitting program. For a product to be an appropriate candidate for splitting, several factors should be considered.[1] Sustained-release, enteric-coated, and other dosage forms where tablet splitting would compromise the product's intended release mechanism should not be considered. The product should be relatively flat-priced across dose or have an acquisition cost to the organization that would offer a savings by splitting the higher doses. To maximize savings, tablet splitting should be preferentially considered for more expensive medications. Using these criteria, VA and other health care organizations may prospectively identify prescription medications where mandated tablet splitting will reduce prescription costs while not compromising patient care.

It should be noted that the VA tablet-splitting program is cost-neutral to patients. The patient copayment is $7 for a 30-day supply, although some patients are exempt from providing a copayment because of financial status or service-connected disabilities. Since copayments are based on days of therapy and not drug costs, VA patients do not have a financial motivation to split tablets. However, patients in other health care systems, particularly those patents who pay out-of-pocket for medications, would likely have a greater incentive to utilize tablet splitting. This motivation would be most pertinent to those products that are flat-priced, enabling patients to purchase twice the drug supply for a given cost.

Limitations

The results of this study generally support the mandatory tablet-splitting policy of the VISN 5 region but are subject to limitations. One limitation is that there are no publicly defined acceptance criteria for half-tablet weight uniformity. Hence, alternative criteria can be considered and applied to our results. In our consideration of the data, we applied criteria that we have used previously.[6] These criteria are more liberal than the USP test for whole tablets, in part since the USP test allows only an initial RSD of no more than 6%, while the criteria that we applied allowed 10% RSD. If an initial 6% RSD limit were applied, several of the products in Table 1 that we found to pass would require further evaluation (i.e., "Stage 2" testing) and could possibly fail. Additionally, half tablets were assessed for dose uniformity immediately after being split; half tablets were not placed back into a prescription vial, where they may be subjected to attrition. At this time, we know of no specific evidence to favor any particular acceptance criteria for weight uniformity of half tablets. It has been suggested that patients, caregivers, and health systems would benefit from public quality standards for half tablets.[6,7]

A second potential limitation of this study is the use of a trained pharmacy student to perform the tablet splitting. It is possible, and even likely, that different outcomes would result, depending on who performed the splitting. It would be perhaps desirable to evaluate the ability of various individuals and patients to split tablets and to elucidate the individual patient factors that contribute to successful tablet splitting. Given the positive results of our study, further research would be desirable to determine if VA patients can obtain similar favorable weight uniformity to better replicate the real-world environment. Other studies have assessed the ability of patients to split tablets. McDevitt et al. evaluated the ability of healthy volunteers to split hydrochlorothiazide tablets by hand.[23] Gender, age, education, or tablet-splitting experience were not found to be predictive of the ability of individuals to split tablets. Peek et al. evaluated the ability of patients to split simvastatin, metoprolol, warfarin, and lisinopril tablets.[24] Individual patients were assigned to one of 4 groups that differed in brand of tablet splitter and whether patients were instructed in the method of tablet splitting. Peek et al. found that both the brand of the tablet-splitting device and instruction improved tablet-splitting accuracy. Patient experience also resulted in more accurate splitting of warfarin tablets.

A third potential limitation was our use of a specific device to split tablets. Peek et al. found that one splitter performed better than another splitter.[24] The suggestion that different tablet-splitting devices can yield markedly different uniformity results reflects our previous anecdotal experience with a tablet-splitting device different from the device used in the present study. In our previous experience, the commercially available tablet splitter appeared to be of lower quality and poor design; a razor blade was simply glued onto a plastic housing at an angle not perpendicular with the plastic housing, resulting, commonly, in properly centered tablets splitting into approximately one third/two third "halves." The poor design and performance of this earlier device caused us to abandon the use of a tablet splitter and rely on splitting tablets with a simple razor blade, by hand.[6] Hence, we suspect that the quality of the tablet splitter can directly affect half-tablet weight uniformity, and our results using the ACE-LIFE Pill Splitter model PS12E may not be applicable to all tablet-splitting devices.

We also did not measure patient outcomes. Tablet splitting could have an adverse effect on patient compliance. Several studies have examined the influence of patient tablet splitting on compliance and generally indicate that most patients accept tablet splitting. For example, Carr-Lopez et al. studied 233 patients, aged 35 to 87 years, who were prescribed 40 mg tablets of lovastatin and instructed to split them into two 20 mg doses.[25] Most patients reported that the tablet splitter was easy

use and did not affect their compliance. However, 6% reported that the tablet splitter was difficult to use, and they would not split tablets even to save money. Mendez et al. found similar results for patients taking half tablets of simvastatin, although 40% of patients believed that splitting would influence compliance.[26] Fawell et al. studied the relationship of tablet splitting and compliance, drug acquisition cost, and patient acceptance for fosinopril sodium.[27] Patients accepted tablet splitting, and the splitting of fosinopril sodium tablets reduced the drug acquisition costs in the health system without affecting patient compliance.

Another potential limitation is the unknown clinical significance of dose variability in half tablets. The focus of our work was on products relevant to the VISN 5 region. Other products of interest may include drugs with a narrower therapeutic index. Dose variability is expected to be of greater potential importance for drugs with a narrow therapeutic index. Warfarin was evaluated here and is considered a narrow therapeutic index drug. Given the small dose variations observed here for warfarin half tablets and the lack of evidence to suggest any adverse clinical effects of such small dose variations, we anticipate tablet splitting of warfarin to have no clinical consequence.

Conclusion

revious observations from experience with razor blade tablet splitting showed that a majority of tablets did not split evenly and that visible tablet features did not predict success or failure of the half tablets to pass the weight-uniformity test. However, our results for weight uniformity in the current study were favorable and generally support the mandatory tablet-splitting policy of the VISN 5 region. We interpret our results to indicate that a tablet-splitting policy is a viable approach to provide patients with dosage forms with acceptable weight uniformity. There is, however, a need for quality standards for half tablets to permit health care providers to better delineate the acceptability of tablet-splitting policies.

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DISCLOSURES

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The Practice of Splitting Tablets

Cost and Therapeutic Aspects

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Abstract

Background: Tablet splitting is used in pharmacy practice to adjust the dose to be administered. It is also being advocated as a method of reducing prescription drug costs.

Methods: The potential for using this practice as a cost-saving method was examined. The top 200 prescription products in Canada were evaluated for their potential for tablet splitting to reduce costs.

The assessment was based on the dosage form (only tablets could be split), availability of dosages in multiples, whether the drug was used for long-term therapy, whether the product was packaged suitably (e.g. oral contraceptives in a therapeutic package), whether pricing structure would allow substantial saving, and the physical nature of the tablets (e.g. whether there were special dose-release characteristics). The products most commonly split in three Canadian pharmacies were compared with the products that had a substantial savings potential. Costs for splitting tablets in the pharmacy and costs of instructing patients to split tablets were calculated.

Results: Savings could be generated from tablet splitting for only 15 of the 200 products. There was little overlap between these 15 products and the products that were most frequently split in the three pharmacies. The costs associated with tablet splitting in the pharmacy were approximately 0.1 Canadian dollars ($Can) per tablet. The cost of instructing a patient to split the tablets was approximately $Can1.

Conclusions: Tablet splitting appears to have limited usefulness as a cost-reduction strategy. Only a small proportion of products are suitable for splitting and have the potential for savings. There are also costs arising from splitting tablets in the pharmacy, or instructing patients to do so, and from wastage of product. There are also issues such as patient compliance and the risk of an incorrect dose being taken that should be considered.

Tablet ('pill') splitting is an accepted practice in dispensing medication. It has been used when a dosage form of the required strength is not available commercially. This is a common clinical problem in prescribing low-dose therapy for elderly patients.[1] More recently, the practice has been used in some countries as a method to control prescription expense. With the increasing cost of medication this practice may become more common.

Splitting tablets for the purpose of providing a lower dose is done under various circumstances, including providing medication for a child or older person when the dosage form is not available in the prescribed strength, when tapering a dose, or when titrating the dose. Tablet splitting is one of many

techniques used by pharmacists and nurses to provide medication in the proper dosage.

A number of medications are used at doses much smaller than those traditionally used. For example, hydrochlorothiazide is commonly used at a dose of 12.5mg, but the lowest dose tablet currently available is 25mg. Thus, patients need to split tablets in order to receive the smaller dose. This approach contributes to a more cost-effective approach to treating hypertension.[2]

Slow titration refers to starting a medication at a low dose and slowly increasing the dose to the target level. One example of the benefits of tablet splitting for slow titration is in patients post-myocardial infarction (MI). Often patients post-MI cannot tolerate full doses of β-blockers used in clinical trials and are often given a very small initial dose of a β-blocker, such as metoprolol 12.5mg, in order to see how they tolerate the drug. If the patient tolerates this dose, the dosage is gradually increased to reach the dosage used in comparative clinical trials. However, the smallest dose metoprolol tablet is 50mg, which requires that the tablet be split into quarters to provide the 12.5mg dose. The procedure of splitting tablets thereby allows for ease of dosage management by the patient, because only one tablet dosage is required. If several different dosages of tablet were used, this would have the potential of increasing the errors in taking medication, as well as increasing the cost of the medication to the patient.

Patients who are receiving anticoagulation therapy with warfarin may require frequent dosage changes to maintain an appropriate level of anticoagulation, especially when starting therapy. Patients are often prescribed warfarin 2mg tablets when therapy is initiated. This allows for modification of dosage by using one or more tablets, or breaking the tablets in half for smaller increments. Instead of purchasing numerous different dosage tablets, the patient would purchase one dosage of tablet, and then adjust the dosage as directed.

The accuracy that can be achieved in splitting tablets varies with the size of the tablet and its characteristics.[3,4] For example, when halving small tablets there was a variation in weight of more than 20 for 44% of the tablet halves. This is outside the compendial limits of variation for tablets. It appears that for reasonable accuracy in dosage, tablet splitting should be restricted to large or scored tablets. This has been confirmed in an evaluation of a commercial product for splitting tablets. The Pill Splitter (LGS Health Products, Beachwood OH) was found to be effective in splitting all the tablets tested, with best results from large tablets (tablets approaching 0.5cm in size take longer to position for cutting) and those that were coated (film rather than sugar coated, for example).[5]

In one small study comparing tablets that were split (40mg atorvastatin) with an equal dose of the formulated product (20mg), there were no differences in clinical outcomes, as measured by low-density lipoprotein cholesterol levels, in patients followed for 12 weeks.[6] This study also demonstrated that there were no significant clinical implications relating to compliance/adherence with therapy when tablets are split.

The patient may be required to perform the tablet splitting and this would be indicated in the label directions, or verbally by the pharmacist. Alternatively, the tablets may be split by the pharmacy staff at the time of dispensing. There do not appear to be any problems of compliance or patient acceptance of therapy when split tablets are used.[7]

Some countries have specifically set out instructions for splitting tablets; for example, Barbados, through the Barbados National Drug Formulary.[8] Some health management organisations (HMOs) in the US also have guidelines for the splitting of tablets to effect savings. An instruction sheet from one HMO entitled 'Half-tablets: cost-effective and easy to do!' states that the purpose is to save money.[9]

The cost savings achieved through tablet splitting may accrue either to the patient, where they must pay for their own medications out of pocket, or to a drug benefit programme. For many drugs, generic products are available at reduced cost. For newly marketed medications that do not yet have generic equivalents (e.g. an HMG-CoA reductase inhibitor, or 'statin'), the splitting of tablets may

provide substantial cost savings for the patient. They may be able to obtain a full prescribed dose of the medication at a fraction of the cost, by obtaining tablets containing twice the required dose and splitting them.

Tablet splitting has several drawbacks.

- *Unsuitability of some dosage forms:* Controlled release tablets have been designed to release the medication in a predictable manner over time. To do this a variety of methods have been used. Some methods, such as the use of coated granules, may be suitable for tablet splitting. Other dosage forms, however, would have their designed features impaired by splitting. The difficulty in assessing the suitability of each controlled dosage form and the probability of impairing their function makes it impractical to include these tablets for tablet splitting.
- *Wastage:* Because of poor technique or tablet characteristics, the tablets may crumble or shatter when splitting is attempted. This leads to wastage of the product, as the tablet fragments cannot be used because of dose inaccuracy. The loss from tablet wastage may significantly decrease the benefits of tablet splitting.
- *Incorrect dose:* For the reasons mentioned above, the patient may split tablets unevenly, resulting in an incorrect dose being administered. This would be a significant concern if it occurred with a drug with a narrow therapeutic index, such as digoxin. While 0.25mg tablets are available, it would be dangerous to have the patient split tablets to provide 0.125mg. It may also be difficult to split irregularly shaped tablets evenly.
- *Confusion/noncompliance:* Even patients who have excellent records of compliance may become confused about their regimen, especially if their medication dose is frequently adjusted or requires splitting tablets. In one reported case, a patient receiving two and a half 1mg warfarin tablets was prescribed 0.5mg warfarin tablets and continued to take two and a half tablets, not realising the difference in dose.[10] A patient may not read the label accurately and take a full tablet instead of splitting the tablet. If the pharmacy supplies the tablets already split, the patient may not realise that the tablets are already split and choose to split the half tablets again, thereby receiving only 50% of the prescribed dose. Patients who require a regimen including split tablets need to be counselled about how to administer and split the tablets. Compliance may be increased by having the pharmacy staff split the tablets and dispense them in an appropriate form of compliance packaging. This would increase the cost of providing the medication.

Older patients or patients with disabilities may have difficulty splitting tablets, either manually or with a tablet splitter.[11,12] Those with vision or manual dexterity problems may find tablet splitting very difficult. In a study of acute geriatric patients, 94 (78.3%) were unable to open a container or break a scored tablet.[11] Even using tablet-splitting devices may be challenging for these patients, because good eyesight and manual dexterity are essential to place the tablet in the cutting device, line it up appropriately, and ensure the tablet is evenly split before administering the product. Patients may also have difficulty splitting tablets if the tablets are not scored.

If they do not receive assistance, patients may become frustrated to the point that they become nonadherent to the prescribed regimen. They may try to adapt their regimen to their abilities, by taking a full tablet every other day. However, this type of alternate-day regimen can be dangerous. Patients must be continually encouraged, counselled and monitored if they are to succeed on a regimen that involves splitting tablets. This requirement for more professional time is a cost that will offset some of the economic gains from tablet splitting.

With the use of tablet splitting as a means of reducing prescription costs, there is a need to analyse the potential benefits and drawbacks to this practice. This paper sets out some of the potential savings available from the practice of tablet splitting, based on the top 200 products on the Cana-

dian market, and factors that constrain the possible savings.

Methods

Cost-Saving Potential

The top 200 prescription drugs in Canada, based on number of prescriptions, were selected to determine the potential for tablet splitting as a mechanism to reduce prescription price.[13] The proportion of tablets suitable for splitting and the cost of the tablets for each dosage were determined for each drug.

The suitability for splitting was determined based on the dosage form (only tablets could be split), availability of dosages in multiples, whether the drug was used for long-term therapy, whether the product was packaged suitably (e.g. oral contraceptives in a therapeutic package), whether the pricing structure would allow substantial saving (more than $Can0.10 per tablet – roughly the salary expense for a pharmacy staff member to split the tablets; 2000 values), whether they had special dose-release characteristics and the nature of the tablets (e.g. spherical or irregular tablets are difficult to split). The cost of a tablet-splitting device ranges from $Can6 to $Can10.

Comparison with Current Practice

Information was sought on the pharmaceutical products that are routinely split in practice. To identify these products, three Canadian (Edmonton) pharmacy managers specialising in geriatric services were asked to prepare a list of products they commonly split. These were then compared with the top 200 products list.

Time Required to Split Tablets in Pharmacy

The time required to split tablets in the pharmacy was determined by using a stopwatch. Two pharmacy students used a tablet splitter to split 20 tablets of four different products selected as a convenience sample. The average time was calculated from these data and was used to calculate the cost to cover the added time cost in tablet splitting. This would be done in cases where the patient was unable to split the tablets accurately.

Time to Counsel Patients on Tablet Splitting

A pharmacy student counselled eight actual patients on tablet splitting. The procedure was timed by the pharmacy student using a stop watch.

Results

Cost-Saving Potential

The top 200 products had a variety of dosage forms, of which 148 were tablets. These tablets consisted of various tablet forms (sugar- or film-coated, sustained-release, sublingual). A number of products were found to be unsuitable for splitting because of their therapeutic characteristics or presentation. This reduced the potential number of products to 127. About 70 of the products were generic or low-cost products that would yield little saving from tablet splitting. For the remaining products, many had dosages that were not in multiples that could be used for tablet splitting, for example a 10mg and a 25mg tablet.

By narrowing the list to medications that are for long-term therapy, tablets that can be easily split and those for which there is a gain of at least 10 cents, the number of drugs was reduced to 15 [enalapril (Vasotec®[1]), warfarin (Coumadin®), simvastatin (Zocor®), pravastatin (Pravachol®), atorvastatin (Lipitor®), lisinopril (Zestril®), fosinopril (Monopril®), lisinopril (Prinivil®), quinapril (Accupril®), risperidone (Risperdal®), sumatriptan (Imitrex®), alendronate (Fosamax®), nefazadone (Serzone®), cilazapril (Inhibace®) and lovastatin (Mevacor®)]. They represent only 14 chemical entities and include four statins and five ACE inhibitors (table I).

The potential savings from tablet splitting for these products are substantial. Many of the products have similar prices for each of the dosages, so

1 Use of tradenames is for product identification only and does not imply endorsement.

Table I. Potential cost savings from tablet splitting of 15 products

Drug	Dose (mg)	Price per tablet (Canadian dollars; 2000 values)	Dose (mg)	Price per tablet	Saving (%)
Quinapril (Accupril®)	5	0.82	10	0.82	50
	20	0.82	40	0.82	50
Cilazapril (Inhibace®)	2.5	0.68	5	0.79	41
Fosinopril (Monopril®)	10	0.79	20	0.95	40
Enalapril (Vasotec®)	2.5	0.68	5	0.68	50
	5	0.68	10	0.96	29
	10	0.96	20	1.16	40
Lisinopril (Zestril®)	5	0.67	10	0.87	34
Lisinopril (Prinivil®)	10	0.87	20	1.05	40
Atorvastatin (Lipitor®)	10	1.16	20	2	38
	20	2	40	2.15	46
Lovastatin (Mevacor®)	20	1.73	40	3.19	8
Pravastatin (Pravachol®)	10	1.15	20	1.79	22
	20	1.79	40	2.15	40
Simvastatin (Zocor®)	5	0.9	10	1.78	1
	10	1.78	20	2.2	38
	20	2.2	40	2.2	50
	40	2.2	80	2.2	50
Risperidone (Risperdal®)	0.25	0.42	0.5	0.7	17
	0.5	0.7	1	0.96	31
	1	0.96	2	1.92	0
	2	1.92	4	3.83	0
Nefazadone (Serzone®)	50	0.73	100	0.8	45
	100	0.8	200	0.93	42
Alendronate (Fosamax®)	5	1.38	10	1.76	42
Sumatriptan (Imitrex®)	50	12.95	100	14.27	45
Warfarin (Coumadin®)	1	0.32	2	0.34	47
	2	0.34	4	0.42	38
	2.5	0.33	5	0.36	45
	5	0.36	10	0.57	19

savings of up to 50% are possible. Most savings are in the range of 30 to 50%. Maximum savings are obtained for quinapril, for which all dosages are priced the same.

Comparison with Current Practice

The list of tablets that were reported to be commonly split in three Edmonton pharmacies is as follows: amlodipine, atenolol, benztropine, calcium (unspecified), carbamazepine, clonazepam, Dyazide®, hydrochlorothiazide, indapamide, loxapine, methylphenidate, metoprolol, oxybutynin, paroxetine, risperidone, sildenafil, sotalol, Stresstabs® (a high potency multivitamin product classified as a dietary supplement), warfarin and zopiclone (table II). The lists from each pharmacy had little overlap. They represent routine medication for chronic disease.

For the listed products that were reported as being split in Edmonton, there is an overlap of only two products from the top 200 products: risperidone and warfarin. Savings were not substantial, with only 4 of 19 showing savings of more than $Can10 for an average prescription representing a 1-month supply of medication. Six of the products did not have double-strength products that would generate savings by splitting.

Time Required to Split Tablets in Pharmacy

The results are presented in table III. The products used for timing were Desyrel® 50mg (trazodone), Norvasc® 10mg (amlodipine besylate),

Novo-cimetine® 600mg (cimetidine) and Apo-Trimip® 25mg (trimipramine maleate).

The cost associated with tablet splitting was based on an hourly rate of $Can60, which is representative of charges for pharmaceutical services in Canada.[14] Based on an average time for tablet splitting of 5 seconds per tablet (table III), the service cost of splitting was $0.0833 per tablet. This indicates that a cost of almost 10 cents per tablet would be incurred to cover the pharmacy cost of splitting tablets. The use of technicians or trained staff to split tablets may reduce the cost. If the patients split the tablets themselves, this pharmacy cost is avoided.

Other costs would be incurred in implementing a tablet-splitting procedure. The first of these is the product expense resulting from wastage when the tablets shatter or break unevenly. This cost is one that both pharmacy and patient might incur. Additional salary cost to cover the added calculation and record keeping is required.

Time to Counsel Patients on Tablet Splitting

Counselling time for eight patients on tablet splitting ranged from 37 to 80 seconds (table IV). The patients ranged in age from 54 to 68 years. For the four patients who had split tablets previously, the average time was 57.5 seconds. The four patients who had not split tablets previously required an average of 64 seconds. Overall, the average time for counselling was 60.75 seconds. At an hourly cost of $Can60, the counselling expense would be about $Can1.00.

Discussion

From this limited sample it appears that in current practice, tablet splitting is more likely to be for clinical, than for economic, reasons. However, there appears to be some benefit in using tablet splitting as a means of reducing drug costs, and the procedure is used widely, both in Canada and elsewhere. The procedure can generate savings, not only for new, expensive products, but also for many products that have moderate costs. In Barbados, a small study of six drugs used in cardiovascular disease showed prescription savings from tablet splitting in the range of 15 to 35% (personal communication, Pamela Payne, 2001 Aug).

Similarly, HMOs in the US seek out savings and insist on tablet splitting for many products. The

Table II. Potential cost savings from tablet splitting in 3 pharmacies

Drug	Dose (mg)	Price per table ($Can; 2000 values)	Dose (mg)	Price ($Can; 2000 values)	Average no. of tablets/prescription	Saving ($Can)
Amlodipine	5	1.23	10	1.82	44	14.08
Atenolol	100	0.11			51	
Benztropine	2	0.02			35	
Carbamazepine controlled release	200	0.21	400	0.42	92	0
Clonazepam	0.05	0.12	1	0.19	49	1.23
Dyazide[a]	0.05				40	
Hydrochlorothiazide	25	0.04	50	0.04	51	1.02
Indapamide	1.25	0.19	2.5	0.3	50	2
Loxapine	50				45	
Metoprolol	50	0.12	100	0.22	111	1.11
Oxybutynin	5				62	
Paroxetine	10	1.49	20	1.59	38	26.41
Risperidone	0.5	0.7	1	0.96	38	8.36
Sildenafil	50	10.8	100	10.8	6	32.4
Sotalol	80	0.59	160	0.65	78	20.67
Warfarin	2	0.34	4	0.42	62	8.06
Zopiclone	75	0.47			34	

a A combination product containing triamterene 50mg and hydrochlorothiazide 25mg; **$Can** = Canadian dollars.

Table III. Average time (sec) to split four different products

Product	Student 1	Student 2
Trazodone (Desyrel®) 50mg	4.05	4.35
Amlodipine (Norvasc®) 10mg	5.4	5.0
Cimetidine (Novo-cimetine®) 600mg	5.5	6.0
Trimipramine (Apo-Trimip®) 25mg	4.1	4.4
Mean time (sec)	4.76	4.94

avoidance of expense by tablet splitting is recommended in the US by various nonprofit groups such the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure, as well as the publication Consumer Reports. An incentive for patients to economise is the requirement that they pay the full cost, or a substantial portion of the costs, of medication that is not covered by a drug benefit programme.

In countries where medication is dispensed in the original treatment pack (thus creating an obstacle to pharmacists splitting tablets for patients), it is possible for patients to realise savings as long as the pricing structure results in similar prices for varying doses. The disincentive for this to occur in many European countries is the extensive health insurance coverage for medication, which requires patients to pay only a portion of the cost. For this reason the use of tablet splitting as a method of generating health cost savings may be appropriate only for some countries.

The potential for using this method to reduce costs is severely restricted by the small number of products suitable for tablet splitting. The practice is largely dependent on the actions and policies of pharmaceutical manufacturers. Changes in pricing policies could create a substantial reduction in possible savings. Pharmaceutical firms also have the capacity to encourage or hinder the practice of tablet splitting by the dosage forms they produce. The number of dosages available, the characteristics of the tablet, the use of controlled-release dosage forms and packaging all have an effect.

Errors involving split tablets are likely to result in double or half the dose being taken, which can be harmful to the patient. Widespread use of tablet splitting may increase the inappropriate use of medication, a problem that is now serious and in need of redress. To minimise problems, there is a need for effective instruction by pharmacy or other healthcare personnel, as well as some form of continual monitoring of drug use to detect inappropriate dosages being taken.

Patients have a major role in understanding the relationship of dosage to dosage forms, so that they are not confused by the splitting of tablets. They should be able to split the tablets easily, either by hand or with a tablet splitter. To achieve the therapeutic and economic benefits from tablet splitting, patients need to be educated on the rationale and procedures of tablet splitting. This process takes time and incurs a cost. For instruction on tablet splitting, counselling takes only about 1 minute. If more detailed counselling were required, based on dosage or disease factors, the time would be longer.

In cases where medication is prepared by the pharmacist, there is less problem with an inappropriate dose being used in an institutional setting, or if the medicine is dispensed in compliance pack-

Table IV. Time required to counsel patients on tablet splitting

Patient age (y)/gender	Drug	Repeat treatment?	Time (sec)
57 M	Hydrochlorothiazide 25mg	Yes	37
61 M	Hydrochlorothiazide 25mg	No	80
67 M	Atenolol 50mg	Yes	69
54 M	Atenolol 50mg	Yes	49
61 M	Atenolol 50mg	No	60
62 M	Paroxetine 20mg	Yes	75
68 F	Paroxetine 20mg	No	57
65 F	Metoprolol 50mg	No	59

F = female; M = male.

aging (weekly medication boxes or bubble packs) for ambulatory use. For ambulatory patients, medication provided without compliance packaging would require some patient instruction. There is, however, a cost generated by the preparation of the medication. At a cost of 10 Canadian cents per tablet for tablet splitting, a prescription of 100 tablets would cost an additional $Can10.00. Compliance packaging would also incur additional costs.

Private or public drug benefit programmes have the greatest potential gain from a general trend towards tablet splitting to save on pharmaceutical expenditures. They can select products where savings will be realised and set out guidelines for the tablet-splitting procedure. There may be substantial cost savings for some expensive products. This is best realised for long-term therapies where the patients can consistently and accurately split the tablets. But it should be realised that major saving on a few products has little effect on the overall expenditure level.

A policy of attempting to implement tablet splitting on a widespread basis as a general approach to cost cutting, however, would be likely to create problems of inappropriate drug use, with resultant toxicity, decreased compliance with therapy and less attention to patient instruction and monitoring. In many cases, the costs incurred in following this approach for some products would be greater than the saving and make the healthcare system less efficient. The combination of administrative policy-making, product evaluation, implementation of procedures and monitoring could lead to substantial administrative overhead costs that would limit savings and increase programme complexity.

Limitations to the generalisability of this study result from local costs and practices that may not be comparable to those in other countries. Local conditions may be conducive to a widespread use of tablet splitting in one area and not in another.

Conclusion

Tablet splitting has a major role in dosage adjustment in a variety of therapeutic situations. However, its potential for cost saving is limited and it is better suited to specific situations than as a method of general cost reduction in pharmaceutical programmes.

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The Potential of Pill Splitting to Achieve Cost Savings

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Objectives: To present a methodology for identifying specific medications for which pill splitting is clinically appropriate and cost saving, to present data from a commercial managed care population on current pill-splitting practices, and to estimate additional cost savings from extended use of this strategy.

Study Design: Retrospective pharmacy claims analysis.

Methods: Pharmacy claims data from a commercial managed care health plan covering 19,000 lives and national drug data were used to compile a list of frequently prescribed medications. Excluding medications in which packaging, formulation, and potential adverse pharmacologic outcomes prohibited splitting, we performed a cost analysis of medications amenable to splitting.

Results: Eleven medications amenable to pill splitting were identified based on potential cost savings and clinical appropriateness: clonazepam, doxazosin, atorvastatin, pravastatin, citalopram, sertraline, paroxetine, lisinopril, nefazadone, olanzapine, and sildenafil. For these medications, pill splitting is currently infrequent, accounting for annual savings of $6200 (or $0.03 per member per month), just 2% of the potential $259,500 (or $1.14 per member per month) that more comprehensive pill-splitting practices could save annually.

Conclusions: Pill splitting can be a cost-saving practice when implemented judiciously using drug- and patient-specific criteria aimed at clinical safety, although this strategy is used infrequently.

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In recent years, the cost of prescription drugs has accelerated drastically. Patients, insurers, and provider networks continue to bear the burden of prescription drug costs, which have increased nearly 60% since 1991 and tripled since 1980.[1]

To alleviate rising prescription drug costs, physicians and providers have used various cost-saving strategies, including the use of generic medications, selection of more cost-effective medications, tiered systems of drug copayments, and formulary restrictions.

One cost-saving strategy that may not have yet reached its potential is pill splitting. Many prescription drugs are available at increased dosages for the same or similar costs as smaller dosages. By prescribing half as many higher strength pills and splitting them to achieve the desired dosage, patients and physician systems can save as much as 50% on the cost of selected medications. As a cost-saving approach, pill splitting has great potential. For example, a patient being treated with 10 mg lisinopril (Zestril; AstraZeneca Pharmaceuticals, Wilmington, DE) will have annual medication costs of $340. By prescribing half the number of 20-mg tablets to be split, medication costs will drop to $180 annually, savings of $160 (47%).[2] Similarly, a recent study focusing on splitting psychotropic medications suggests the potential for annual national savings of $1.4 billion.[3]

Pill splitting is a well-established medical practice,[4] not uncommon in prescribing pediatric[5] or geriatric dosages.[6] However, fears of inaccurate dosing, noncompliance, and physical inability to split tablets have discouraged physicians and patients from adopting this practice. Opponents of pill splitting have cited unpredictable effects on the stability of the drug, loss of drug due to powdering, creation of uneven doses, lack of physical strength and dexterity, poor eyesight, reduced cognitive ability, and

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This study was supported by the Massachusetts General Hospital Primary Care Operations Improvement Initiative.

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lack of instruction as arguments against pill splitting.[4] However, prior studies suggest that most patients are able to accurately split pills with minimal loss of tablet content.[4,7] With some notable exceptions, the chemical stability of most tablet formulations is not substantially altered by pill splitting.[5] Concerns also have been expressed over patient adherence. There is a fear that prescribing higher dosages that require tablets to be halved will lower adherence: patients may not be willing to take the time to split a pill before taking it or may be unable to split a pill. Objectively, however, 1 study found that splitting tablets had no effect on adherence.[8] It was further suggested that tablet splitting might increase adherence by reducing the cost barrier faced by some patients.[8]

Pill splitting is safer and easier when drug- and patient-specific criteria have been met. Medications should not be considered when packaging and pricing structure do not make splitting cost effective or even possible. Medications should not be split if splitting could result in adverse pharmacologic outcomes. Such medications include those with enteric coatings, extended-release formulations, a narrow therapeutic window, or a short half–life-to-dosing ratio. The use of pill-splitting devices can make splitting tablets easier for patients and often yields more accurate doses,[9] and some physical properties of medications such as scoring, shape, and size affect the ease and accuracy of splitting.[7]

Patients should be instructed by pharmacists how to accurately split tablets manually or how to use a pill-splitting device. In most cases, patients should be comfortable with splitting their own medication, and they should be free from physical impairments, including poor eyesight, loss of a limb, tremors, debilitating arthritis, or any other condition that might hinder accurate pill splitting. Pill splitting by pharmacists may still be a viable option for impaired patients in selected states.[4] Although consideration of these many factors suggests that pill splitting can be undertaken without compromising patient safety, explicit evaluation of this question has not been undertaken.

Pill splitting also has the advantages of making newer and expensive medications available to more people who might not otherwise be able to afford them, allowing physicians to individualize a patient's dosage when the medication is not available in the desired dosage, and offering cost savings without risking a withholding of needed services. Pill splitting for pediatric patients may have specific advantages regarding dosage, but may also require special caution.

Though a recent study suggests that pill splitting may be frequent in long-term care facilities,[6] little is known about actual patterns of tablet splitting, particularly in ambulatory settings. This report describes a methodology for identifying medications amenable to pill splitting based on specific criteria, and uses pharmacy claims data to gauge current pill-splitting practices and the potential for additional cost savings.

METHODS

We investigated pill splitting within a commercial managed care population of 19,000 covered lives served by primary care physicians affiliated with the Massachusetts General Hospital (MGH). This population consisted of working-age beneficiaries receiving employer-based health insurance in the Boston metropolitan area.

We sought to identify specific medications for which pill splitting would be appropriate and cost saving in 2:1 splitting ratios; to determine current patterns of pill splitting among MGH physicians, to estimate the potential cost savings that would result from pill splitting; and to recommend guidelines for safe pill-splitting prescribing practices.

Pharmacy claims data from January 1, 2000, through August 30, 2000, were available for managed care members with MGH primary care providers. We compiled a list of the 265 most frequently prescribed proprietary and generic medications, both nationally[2] and within the MGH population. To determine medications amenable to splitting, we evaluated each medication using cost- and pharmacologic-specific criteria. Included were cost savings per dosage increase, based on the average wholesale price and actual costs to the health plan, pharmacokinetic interactions and therapeutic window, packaging, and formulation. Physical properties such as scoring and tablet size also were considered, although they were not necessarily determining factors for inclusion in this study.

Preliminary review of the 265 most frequently prescribed medications allowed us to eliminate 125 medications because pill splitting was not feasible. Among the most common reasons were that medications were available in only one dosage, that the medication was administered non-orally, that a capsule or other nonsplittable form was used, and that the tablets were prepackaged. Commonly prescribed medications available in a single dose

included fexofenadine (Allegra; Aventis Pharmaceuticals, Parsippany, NJ), oxaprozin (Daypro; G. D. Searle & Co., Chicago, IL), raloxifene (Evista; Eli Lilly and Company, Indianapolis, IN), and tramadol (Ultram; Ortho-McNeil Pharmaceutical, Raritan, NJ). Common nonoral medications included corticosteroid and β-agonist inhalers. Capsule formulations among frequently prescribed drugs include terazosin (Hytrin; Abbott Laboratories, Inc, North Chicago, IL), fluvastatin (Lescol; Novartis Pharmaceuticals Corporation, East Hanover, NJ), valsartan (Diovan; Novartis Pharmaceuticals Corporation, East Hanover, NJ), fluoxetine (Prozac; Eli Lilly and Company, Indianapolis, IN), and omeprazole (Prilosec; AstraZeneca Pharmaceuticals, Wilmington, DE). Oral contraceptives are the most common examples of prepackaged medications.

The remaining 140 medications were evaluated based on potential cost savings on a per-dosage basis. For continued consideration, a medication was required to have cost savings through splitting that exceeded 25% and/or $0.40 per dosage ($0.20 for generic medications) based on average wholesale price.[2] Of these 140 medications, 61 were eliminated because splitting offered no or minimal cost savings. Examples of commonly used medications that were eliminated because of the lack of per-dosage cost savings through pill splitting included buspirone (BuSpar; Bristol-Myers Squibb Company, Princeton, NJ), metformin (Glucophage; Bristol-Myers Squibb Company, Princeton, NJ), and famotidine (Pepcid; Johnson & Johnson/Merck, Fort Washington, PA).

Using the 1999 and 2001 *American Hospital Formulary Service Drug Information* indices,[10] the 79 remaining medications were evaluated for potential adverse pharmacologic effects. Each medication was screened based on toxicity, rate of absorption, elimination half-life, and therapeutic window. Nine medications with a potential for adverse consequences from splitting were excluded based on manufacturer warning against pill breakage (eg, nitroglycerin [Nitrostat; Parke-Davis, Morris Plains, NJ]), nonproportional combination medications (amoxicillin-clavulanic acid [Augmentin; SmithKline Beecham, Philadelphia, PA]), narrow therapeutic window (eg, warfarin), or rapid half–life-to-dosing ratio (eg, tolterodine [Detrol; Pharmacia & Upjohn, Peapack, NJ]). The latter criteria refers to medications with elimination half-lives short enough relative to the dosing frequency to raise potential concerns about fluctuations in serum concentrations should splitting be inaccurate. Once-daily sertraline, with a half-life of 25 to 26 hours,[10] is an example of a medication with a substantial pharmacokinetic buffer against inaccurate pill splitting. Olanzapine was included because splitting is feasible as long as the split tablet is used within a week of splitting.

Twenty-two additional medications with extended-release formulations were excluded, as altering these medications' physical properties by splitting could negatively impact their pharmacokinetics. Examples of extended-release formulations included felodipine (Plendil; AstraZeneca Pharmaceuticals, Wilmington, DE), extended-release bupropion (Wellbutrin SR; Glaxo Wellcome, Inc, Research Triangle Park, NC), extended-release nifedipine (Procardia XL; Pfizer Inc, New York, NY; Adalat CC; Bayer Corporation, West Haven, CT), and isosorbide mononitrate (Imdur; Key Pharmaceuticals, Inc, Kenilworth, NJ).

A detailed cost analysis of the 48 remaining medications using data from the available pharmacy claims records allowed us to determine actual cost, current rates of pill splitting among MGH physicians, and potential savings from extended use of this strategy. Eliminating those medications with minimal usage in the MGH population, we identified 11 recommended medications for which pill splitting is clinically appropriate and cost saving. Enalapril (Vasotec; Merck & Co. West Point, PA), nefazadone (Serzone; Bristol-Myers Squibb Company, Princeton, NJ), mirtazapine (Remeron; Organon, Inc, West Orange, NJ), zafirlukast (Accolate; AstraZeneca Pharmaceuticals, Wilmington, DE), and clarithromycin (Biaxin; Merck & Co. West Point, PA) were examples of medications that could have been associated with cost savings if they were used more frequently in the MGH system.

To calculate current rates of pill splitting for these medications, we used the following methods: for each daily dose of each medication, we calculated the proportion of prescriptions for which 2-to-1 splitting was implied by the number of pills provided and the days of therapy supplied by the prescription. For example, for all patients prescribed lisinopril 10 mg per day, we compared the number achieving this dose via 10-mg tablets (30 tablets provided for 30 days) with the number achieving this dose via 20-mg tablets split 2-to-1 (15 tablets provided for 30 days). For each medication, we reported the aggregate rate of pill splitting across all possible 2-to-1 splitting possibilities. During our investigation, no organizational efforts were in place to promote pill splitting.

Our cost analysis was based on usage volume and the actual cost of select medications in a commercial HMO population. Our unit of analysis was the prescribed daily dose (mg/day) for each of the selected medications, whereas our outcome measures were the cost savings realized from halving higher-strength tablets to achieve the desired dosage. To estimate current costs and potential savings, we extracted the total number of days of therapy prescribed for each medication at each dosage for all patients as well as the total number of days of therapy for each medication if higher-strength pills were split to achieve the desired dosage. We annualized our 8 months of data to represent expected utilization and costs for a full year. An annualized cost analysis indicated those medications for which sizable current or future cost savings could be expected from pill splitting.

Observed and potential cost savings were calculated using the following equations:

Table. Potential Cost Savings from Pill Splitting in a Commercial HMO Health Plan

Drug and Daily Dose (mg)		Cost in Health Plan Contract			Observed Occurrences		
		Per Pill ($)	If Higher-Strength Pill Is Split ($)	Annual No. of Prescriptions	No. of Prescriptions From Splitting	Observed Annual Savings ($)	Potential Annual Savings ($)
Clonazepam	0.5	0.40	0.24	380	-	0	1456
	1	0.47	0.26	79	-	0	510
Doxazosin (Cardura)	1	0.97	0.48	58	-	0	1207
	2	0.95	0.54	105	11	224	2320
	4	1.00	0.52	76	-	0	146
Citalopram (Celexa)	20	1.90	1.02	890	66	2409	25,758
Atorvastatin (Lipitor)	10	1.77	1.33	2184	3	120	44,746
	20	2.68	1.54	1121	-	0	62,465
Paroxetine (Paxil)	10	2.19	1.15	281	17	712	11,176
	20	2.19	1.21	468	-	0	15,202
Pravastatin (Pravachol)	10	2.03	1.09	88	-	0	4056
	20	2.17	1.74	481	-	0	11,209
Nefazodone (Serzone)	50	1.16	0.60	12	-	0	242
	100	1.19	0.60	33	-	0	565
Sildenafil (Viagra)	25	8.54	4.27	37	-	0	610
	50	8.52	4.27	513	-	0	8461
Lisinopril (Zestril)	2.5	0.55	0.45	85	20	123	415
	5	0.85	0.55	566	9	99	8265
	10	0.88	0.47	1214	-	0	23,754
	20	0.93	0.67	716	-	0	9708
Sertraline (Zoloft)	25	2.11	1.15	87	12	526	2656
	50	2.12	1.14	616	75	1669	20,535
Olanzapine (Zyprexa)	2.5	4.26	2.53	38	3	263	2302
	5	5.09	3.85	52	2	57	1752
Total cost savings						**$6202**	**$259,516**

Daily dosages reported here can be achieved as a whole tablet or from splitting a higher strength tablet in half. The highest reported daily dosage for each drug can be achieved from splitting a higher strength tablet not shown in the table.

Observed annual savings = (savings per day of therapy) × (# of observed annual days of therapy achieved from pill splitting)

Potential annual savings = (savings per day of therapy) × (total annual days of therapy)

RESULTS

Top Drugs for Splitting

We identified 11 medications for which pill splitting was clinically appropriate and could result in significant cost savings (**Table**). Of these medications, many are used for treatment of psychiatric disorders: clonazepam, citalopram (Celexa; Forest Pharmaceuticals, Inc, St. Louis, MO), paroxetine (Paxil; SmithKline Beecham, Philadelphia, PA), nefazadone, sertraline (Zoloft; Pfizer, Inc, New York, NY), and olanzapine (Zyprexa; Eli Lilly and Company, Indianapolis, IN). Also common were medications for lipid lowering: atorvastatin (Lipitor; Pfizer, Inc, New York, NY) and pravastatin (Pravachol; Bristol-Meyers Squibb Company, Princeton, NJ); and for hypertension: doxazosin (Cardura; Pfizer, Inc, New York, NY) and lisinopril. In addition, sildenafil (Viagra; Pfizer, Inc, New York, NY), a drug for erectile dysfunction, was included.

Of the 11 medications, 7 (70%) are scored: clonazepam, doxazosin, citalopram, paroxetine, nefazadone, lisinopril, and sertraline. The potential average cost savings from splitting was 36%. Cost savings ranged from 18% for lisinopril (2.5 mg dose) to 50% for doxazosin (1 mg), nefazadone (100 mg), and sildenafil (25 and 50 mg). Seventy-five percent (18 of 24) of the possible prescribed daily dosages for these medications could yield cost savings of at least 40% per pill.

Pill Splitting Is Currently Infrequent

Although pill splitting was used for a sizable number of HMO members, this practice was relatively infrequent. Splitting was most frequent for sertraline at a dose of 50 mg/day, for which 75 (12%) prescriptions were made from 100-mg tablets to be taken one half per day, compared with 616 (88%) receiving one 50-mg tablet once per day. Other medications for which splitting occurred were citalopram (8%), doxazosin (4%), and paroxetine (2%). Pill splitting was either negligible or not observed for the other selected medications.

Current and Potential Cost Savings

Among the selected 11 medications, we calculated that current pill-splitting practices saved $6200 on an annualized basis, an equivalent of only $0.03 per member per month. The largest contributor was citalopram ($2400). Current cost savings, however, represent only 2.4% of the potential savings that could result from pill splitting among these 11 medications. Full use of tablet splitting for these drugs would generate $259,500 in savings annually (or $1.14 per member per month). The largest potential contributors to cost savings were atorvastatin ($107,200), lisinopril ($42,100), paroxetine ($26,400), citalopram ($25,700), sertraline ($23,200), and pravastatin ($15,300). Because not all patients should be considered for pill splitting, achievable savings would be less than these projections, although this report does offer a useful gauge of cost savings using this strategy.

DISCUSSION

Based on specific criteria focused on safety and frequency, we have identified 11 medications in which extended use of pill splitting could be cost saving for a commercial HMO plan. Of these medications, a preponderance were used to treat psychiatric disorders, hypertension, and hyperlipidemia. The selected medications shared relatively wide therapeutic windows, long half–life-to-dosing ratios, and substantial potential for cost savings. Pill splitting is currently infrequent among MGH physicians, accounting for only $6200 in savings annually, just 2.4% of the potential $259,500 that could be saved from extended use of this cost-reduction strategy for the selected medications. This represents overall savings of 36% off the costs of these selected medications.

A recent lawsuit alleging that a mandatory pill-splitting program adopted by one of the nation's largest health maintenance organizations jeopardized patient safety[11] highlights an important point about appropriate pill splitting: although the practice can save money, pill splitting should be considered only in the context of specific patient-physician assessment and discussion. Review of these legal issues suggests that physicians can reduce the liability risks associated with pill splitting by judiciously limiting pill splitting to those medications and patients for whom it is medically appropriate and by engaging in a candid discussion of the requirements, costs, and benefits of a pill-splitting regimen.

Pill splitting can be expected to be relatively safe when drug- and patient-specific criteria have been met. In addition to appropriate diialog between the

physician and the patient, the following medication characteristics should be considered in selecting medications for splitting:

- Wide therapeutic windows ensure a buffer against potential fluctuations in dosing that could occur because of inaccurate tablet splitting. This includes medications with a relatively large ratio of drug concentrations producing significant undesired effects to those producing desired effects.
- Fluctuations from misdosing also can be minimized by medications that have a long half-life relative to the frequency of dosing because steady-state drug levels are less sensitive to potential variation in individual doses.
- Drugs that have enteric coatings or that are formulated as extended release should not be split.
- Drugs that are prepackaged, such as oral contraceptives, should not be split.
- Medications that do not have a pricing structure that makes splitting cost effective should not be considered.
- Physical properties of medications affect the ease and accuracy of splitting. For example, tablets that are deeply scored or scored on both sides are easier to split than unscored tablets.[7]

Our list of medications incorporated these characteristics, as well as several others that were specific to our setting, including frequency of prescribing and pricing considerations. Whereas other systems may derive somewhat different lists of medications, the foundation for these decisions should always begin with drug characteristics.

Patient-specific characteristics are also vital to consider in tablet splitting. Patients should be willing and able to be instructed by pharmacists on how to accurately split tablets or in the use of a pill-splitting device and they should be comfortable with splitting their own medication. Additionally, patients should have no physical or cognitive impairments that could impede accurate pill splitting or reliable dosing once pills are split. While some states prohibit pharmacists from splitting tablets,[4] pill splitting may still be a viable option for some impaired patients in selected states. For example, regulations controlling pharmacists do not include such a prohibition in Massachusetts, California, Oregon, and New York, among other states. Even where legal, however, lack of reimbursement to pharmacies for pill splitting may constrain the willingness of pharmacists to perform splitting.

The beneficiary of the cost savings generated by tablet splitting will vary depending on the system of reimbursement. Self-pay patients or patients with capped pharmacy benefits will reduce their out-of-pocket expenses by splitting their pills. In other instances, physician systems or health insurance plans will realize the cost savings, as was the case with the population that we analyzed. For patients who would not otherwise benefit, it would be ideal if they could be offered an incentive to use split dosages (eg, a reduction in their copayment).

Out of convenience, we have used data from a commercial health plan, although data from other types of plans could augment our analysis. For example, information on a Medicare population would be appropriate given that elderly patients have greater medication use and experience greater out-of-pocket costs that could be diminished through pill splitting.

Limitations

Although we lack the information needed to estimate precisely the proportion of patients who are unwilling or unable to split pills, this proportion is likely to be smaller within an employed population compared with other populations. In our population, we estimated that approximately 10% to 30% of patients would be unable or unwilling to make use of prescriptions that require pill splitting. Our results, from a large academic medical center and its physicians, may not reflect current practices and potential cost savings in other practice settings. We focused only on medications that were preferred in the MGH managed care plan. This tactic excluded several drugs for which significant savings could be realized in other settings (ie, lisinopril as Prinivil was included, but not Zestril). We focused only on 2-to-1 splitting ratios, although savings may be significant with other dosing ratios (eg, prescribing 75 mg sertraline from splitting three 50-mg tablets over 2 days rather than three 25-mg tablets in one day).

We recognize that the potential cost savings as reported here might not be fully achievable, as pill splitting will not be appropriate for every patient. A number of factors may cause actual savings to fall below those potentially achievable, including a patient's unwillingness to accept split-dosing prescriptions, patient inability to split pills (either through self-splitting or through a pharmacist), and lack of familiarity by prescribers. Although we lack information needed to estimate the proportion of patients that fall into these categories, this proportion is likely smaller within a employed population compared with other populations.

Although many factors suggest that more widespread pill-splitting practices could be adopted without compromising patient safety, it was beyond the scope of this study to evaluate the safety of pill splitting in our population either currently or for our projections of increased splitting. A long-term consideration may be that consistent and widespread adoption of tablet splitting might result in pharmaceutical pricing strategies that eventually eliminate the advantages of splitting. More likely, however, is that some segments of the market for pharmaceuticals (eg, managed care or self-pay) may adopt pill splitting more than others.

Implications

Our analysis has indicated that significant cost savings are possible through tablet splitting for a set of medications selected using explicit criteria. We recommend that physicians talk with patients, review their medications, work with them to assess whether pill splitting is a viable option, and use this strategy when it can be carried out safely. The cost savings from this underused practice are significant and, if implemented judiciously, this strategy presents an opportunity to reduce healthcare costs without compromising quality.

Acknowledgments

We thank Dana R. Brakman Reiser, formerly of the Office of the General Counsel, Partners HealthCare System, for her assistance and legal review of material presented in this report.

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Agenda Item K

Strategic Plan Update

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STATE AND CONSUMERS AFFAIRS AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
ARNOLD SCHWARZENEGGER, GOVERNOR

March 26, 2007

To: Members, Legislation and Regulation Committee

Subject: Update of the Committee's 2007-08 Strategic Plan

Last July, the board finalized its strategic plan for 2006-2011. However, each year in the spring, the board revises its plan to keep it current. It is time to start this review.

At this meeting, the Legislation and Regulation Committee will have the opportunity to revise its strategic plan, if warranted.

At the April Board Meeting, the board will review any modifications to the strategic plan recommended by each committee for development of the 2007-08 strategic plan (completing the annual updating process).

The last activity update of the Legislation and Regulation Committee's strategic plan follows this page.

LEGISLATION AND REGULATION COMMITTEE

Goal 3: Advocate legislation and promulgate regulations that advance the vision and mission of the Board of Pharmacy.

Outcome: Improve the health and safety of Californians.

Objective 3.1	Annually identify and respond with legislative changes to keep pharmacy laws current and consistent with the board's mission.
Measure:	100 percent successful enactment of promoted legislative changes
Tasks:	1. Secure extension of board's sunset date (SB 1476). *Sept. 30, 2006:* *Governor signs SB 1476 which delays the board's sunset date two years (until 2010), and requires the board's sunset report in 2008.* 2. Sponsor legislation to update pharmacy law (SB 1475). *Sept. 30, 2006:* *Governor signs SB 1475 containing provisions that:* *(a) Allow a check-off box on electronic prescriptions that if marked by a prescriber, would prevent generic substitution at a pharmacist's discretion (B&P 4073).* *(b) Clarify requirements for reporting to the board when a licensee is impaired to the extent it affects the licensee's safe practice or who has stolen or diverted drugs (B&P 4104).* *(c) Establish the authority to issue a temporary sterile injectable compounding license following a change in ownership (B&P 4127.8)* *(d) Exempt government-owned wholesalers from having to post a $100,000 bond (B&P 4162).* *(e) Exempt drug manufacturers who hold a biologics license application from the FDA from having to post a $100,000 bond otherwise required for nonresident wholesalers (B&P 4162.5).* *(f) Make technical changes in the licensure requirements for clinics (B&P 4180 - 4182, 4190 - 4192).* 3. Advocate the board's role and its positions regarding pharmacists' care and dispensing of dangerous drugs and devices (AB 2408). *Sept. 30, 2006:* *Governor signs AB 2408. Amendments taken in August remove provisions that would have described the professional services provided by pharmacists, and authorized pharmacists outside California to provide pharmacists' care services to patients in California if licensed here or working within the framework of a nonresident pharmacy. Remaining provisions restructure pharmacist protocol provisions and several other changes.* 4. Secure statutory standards for pharmacies that compound medications (AB 595). *Aug. 2006:* *Amendments made to remove opposition of DHS regarding pharmacy contracting with another pharmacy for compounded drugs triggers opposition from pharmacy organizations. Board drops AB 595, but will advance regulations developed for compounding pharmacies in the future.* *Dec. 2006:* *Licensing Committee evaluates proposed compounding regulations developed in 2004. Some modifications may be needed.*

	5. Secure implementation of e-pedigrees on prescription drugs dispensed in California (SB 1476). *Sept. 30, 2006:* *Governor signs SB 1476 which contains board amendments to delay implementation of the e-pedigree requirements until 2009, or upon board action, until 2011. Amendments also require interoperability, serialization, returned drug products to retain the initiating pedigree, require notice to the board of suspected or actual counterfeiting, and continuation of the pedigree through repackaging operations.*
Objective 3.2 Measure:	Annually identify and respond with regulatory changes to keep pharmacy regulations current and consistent with the board's mission. Percentage successful enactment of promoted regulatory changes
Tasks:	1. Authorize technicians to check technicians in inpatient pharmacies with clinical pharmacist programs (sections 1793.7-1793.8). *Aug. 2006:* *Rulemaking file compiled and undergoing review by the Department of Consumer Affairs.* *Nov. 2006:* *Rulemaking file submitted to the office of Administrative Law* 2. Authorize the use of prescription drop boxes and automated delivery machines for outpatient pharmacies (sections 1713 and 1717(e)). *Aug. 2006:* *Rulemaking file compiled and undergoing review by the Department of Consumer Affairs.* *Jan. 2007:* *Regulation takes effect following approval by the office of Administrative Law.* *Jan. 4, 2007:* *Regulation takes effect approved by the office of Administrative Law.* 3. Make technical changes in pharmacy regulations to keep the code updated. Section 1706.2 criteria for abandonment of files *Dec. 2006:* ***Board notices regulation for 45 days of public comment.*** Section 1775.4 contested citations *Dec. 2006:* ***Board notices regulation for 45 days of public comment.*** Section 1709.1 designation of pharmacist-in-charge Section 1780 standards for wholesalers Section 1780.1 standards for veterinary food animal drug retailers Section 1781 exemption certificate Section 1786 exemptions 4. Repeal the requirement to post a notice regarding electronic files (section 1717.2). *July 2006:* *Regulation released for 45 days of public comment. Action to be taken at the October Board Meeting.* *Oct. 2006:* *Board approves regulation and compiles rulemaking file. File submitted to the Department of Consumer Affairs to initiate Administration review.* 5. Revise and update Disciplinary Guidelines revision and update (section 1760). *Aug. 2006:* *Final changes to Disciplinary Guidelines being compiled by staff.* *Dec. 2006:* *Disciplinary Guidelines is being reformatted into strikeout and underscore version for eventual release for public comment.* 6. Self-assessment of a wholesaler by the designated representative (section 1784). *July 2006:* *Regulation released for 45 days of public comment. Action to be taken at the October Board Meeting.* *Oct. 2006:* *Board approves regulation and compiles rulemaking file. File submitted to the Department of Consumer Affairs to initiate Administration review.*

	7. Exempt the address of records of interns from display on the board's Web site (section 1727.1). *Sept. 2006:* *Office of Administrative Law approves rulemaking. Regulation takes effect October 2006.* 8. Modification of building standards for pharmacies – rulemaking by the California Building Standards Commission. *July 2006:* *Board notified that a new procedure now exists for adopting building standards. Staff will pursue these procedures in 2007.*
Objective 3.3	Review 5 areas of pharmacy law for relevancy, currency and value for consumer protection by June 30, 2011.
Measure:	Number of areas of pharmacy law reviewed
Tasks:	

Agenda Item K

Strategic Plan Update

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At this meeting, the Legislation and Regulation Committee will have the opportunity to revise its strategic plan, if warranted.

At the April Board Meeting, the board will review any modifications to the strategic plan recommended by each committee for development of the 2007-08 strategic plan (completing the annual updating process).

The last activity update of the Legislation and Regulation Committee's strategic plan follows this page.

LEGISLATION AND REGULATION COMMITTEE

Goal 3: Advocate legislation and promulgate regulations that advance the vision and mission of the Board of Pharmacy.

Outcome: Improve the health and safety of Californians.

Objective 3.1	Annually identify and respond with legislative changes to keep pharmacy laws current and consistent with the board's mission.
Measure:	100 percent successful enactment of promoted legislative changes
Tasks:	1. Secure extension of board's sunset date (SB 1476). *Sept. 30, 2006:* *Governor signs SB 1476 which delays the board's sunset date two years (until 2010), and requires the board's sunset report in 2008.* 2. Sponsor legislation to update pharmacy law (SB 1475). *Sept. 30, 2006:* *Governor signs SB 1475 containing provisions that:* *(a) Allow a check-off box on electronic prescriptions that if marked by a prescriber, would prevent generic substitution at a pharmacist's discretion (B&P 4073).* *(b) Clarify requirements for reporting to the board when a licensee is impaired to the extent it affects the licensee's safe practice or who has stolen or diverted drugs (B&P 4104).* *(c) Establish the authority to issue a temporary sterile injectable compounding license following a change in ownership (B&P 4127.8)* *(d) Exempt government-owned wholesalers from having to post a $100,000 bond (B&P 4162).* *(e) Exempt drug manufacturers who hold a biologics license application from the FDA from having to post a $100,000 bond otherwise required for nonresident wholesalers (B&P 4162.5).* *(f) Make technical changes in the licensure requirements for clinics (B&P 4180 - 4182, 4190 - 4192).* 3. Advocate the board's role and its positions regarding pharmacists' care and dispensing of dangerous drugs and devices (AB 2408). *Sept. 30, 2006:* *Governor signs AB 2408. Amendments taken in August remove provisions that would have described the professional services provided by pharmacists, and authorized pharmacists outside California to provide pharmacists' care services to patients in California if licensed here or working within the framework of a nonresident pharmacy. Remaining provisions restructure pharmacist protocol provisions and several other changes.* 4. Secure statutory standards for pharmacies that compound medications (AB 595). *Aug. 2006:* *Amendments made to remove opposition of DHS regarding pharmacy contracting with another pharmacy for compounded drugs triggers opposition from pharmacy organizations. Board drops AB 595, but will advance regulations developed for compounding pharmacies in the future.* *Dec. 2006:* *Licensing Committee evaluates proposed compounding regulations developed in 2004. Some modifications may be needed.*

	5. Secure implementation of e-pedigrees on prescription drugs dispensed in California (SB 1476). *Sept. 30, 2006:* *Governor signs SB 1476 which contains board amendments to delay implementation of the e-pedigree requirements until 2009, or upon board action, until 2011. Amendments also require interoperability, serialization, returned drug products to retain the initiating pedigree, require notice to the board of suspected or actual counterfeiting, and continuation of the pedigree through repackaging operations.*
Objective 3.2 Measure:	Annually identify and respond with regulatory changes to keep pharmacy regulations current and consistent with the board's mission. Percentage successful enactment of promoted regulatory changes
Tasks:	1. Authorize technicians to check technicians in inpatient pharmacies with clinical pharmacist programs (sections 1793.7-1793.8). *Aug. 2006:* *Rulemaking file compiled and undergoing review by the Department of Consumer Affairs.* *Nov. 2006:* *Rulemaking file submitted to the office of Administrative Law* 2. Authorize the use of prescription drop boxes and automated delivery machines for outpatient pharmacies (sections 1713 and 1717(e)). *Aug. 2006:* *Rulemaking file compiled and undergoing review by the Department of Consumer Affairs.* *Jan. 2007:* *Regulation takes effect following approval by the office of Administrative Law.* *Jan. 4, 2007:* *Regulation takes effect approved by the office of Administrative Law.* 3. Make technical changes in pharmacy regulations to keep the code updated. Section 1706.2 criteria for abandonment of files *Dec. 2006:* ***Board notices regulation for 45 days of public comment.*** Section 1775.4 contested citations *Dec. 2006:* ***Board notices regulation for 45 days of public comment.*** Section 1709.1 designation of pharmacist-in-charge Section 1780 standards for wholesalers Section 1780.1 standards for veterinary food animal drug retailers Section 1781 exemption certificate Section 1786 exemptions 4. Repeal the requirement to post a notice regarding electronic files (section 1717.2). *July 2006:* *Regulation released for 45 days of public comment. Action to be taken at the October Board Meeting.* *Oct. 2006:* *Board approves regulation and compiles rulemaking file. File submitted to the Department of Consumer Affairs to initiate Administration review.* 5. Revise and update Disciplinary Guidelines revision and update (section 1760). *Aug. 2006:* *Final changes to Disciplinary Guidelines being compiled by staff.* *Dec. 2006:* *Disciplinary Guidelines is being reformatted into strikeout and underscore version for eventual release for public comment.* 6. Self-assessment of a wholesaler by the designated representative (section 1784). *July 2006:* *Regulation released for 45 days of public comment. Action to be taken at the October Board Meeting.* *Oct. 2006:* *Board approves regulation and compiles rulemaking file. File submitted to the Department of Consumer Affairs to initiate Administration review.*

	7. Exempt the address of records of interns from display on the board's Web site (section 1727.1). *Sept. 2006:* *Office of Administrative Law approves rulemaking. Regulation takes effect October 2006.* 8. Modification of building standards for pharmacies – rulemaking by the California Building Standards Commission. *July 2006:* *Board notified that a new procedure now exists for adopting building standards. Staff will pursue these procedures in 2007.*
Objective 3.3 Measure:	Review 5 areas of pharmacy law for relevancy, currency and value for consumer protection by June 30, 2011. Number of areas of pharmacy law reviewed
Tasks:	